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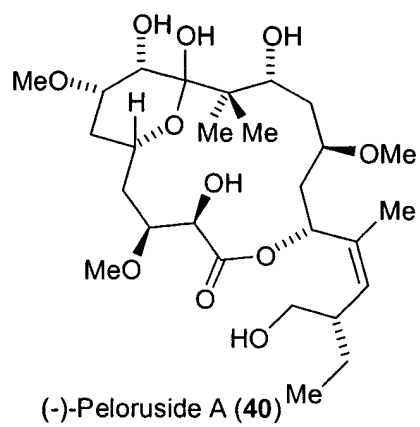


FIG. 1

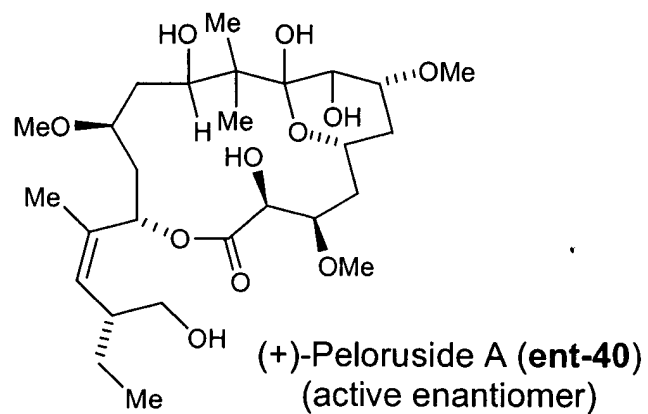


FIG. 2

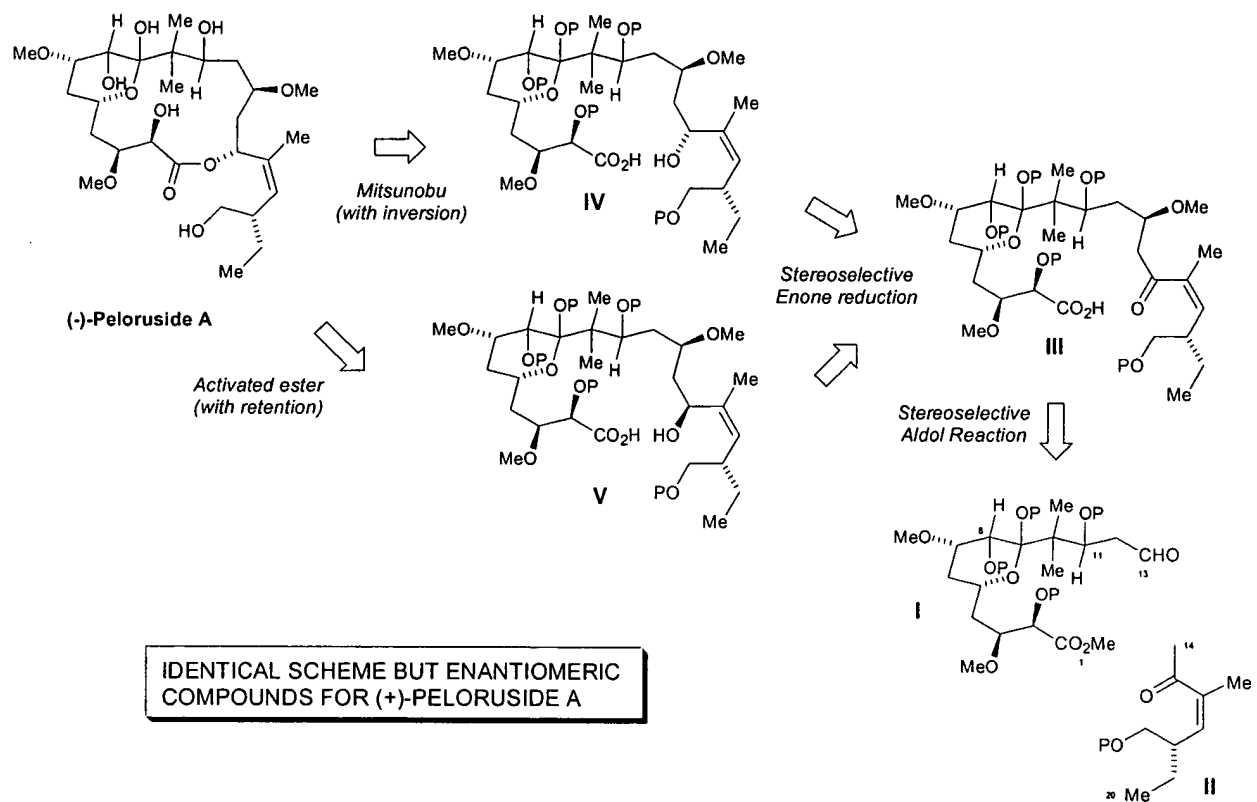


FIG. 3

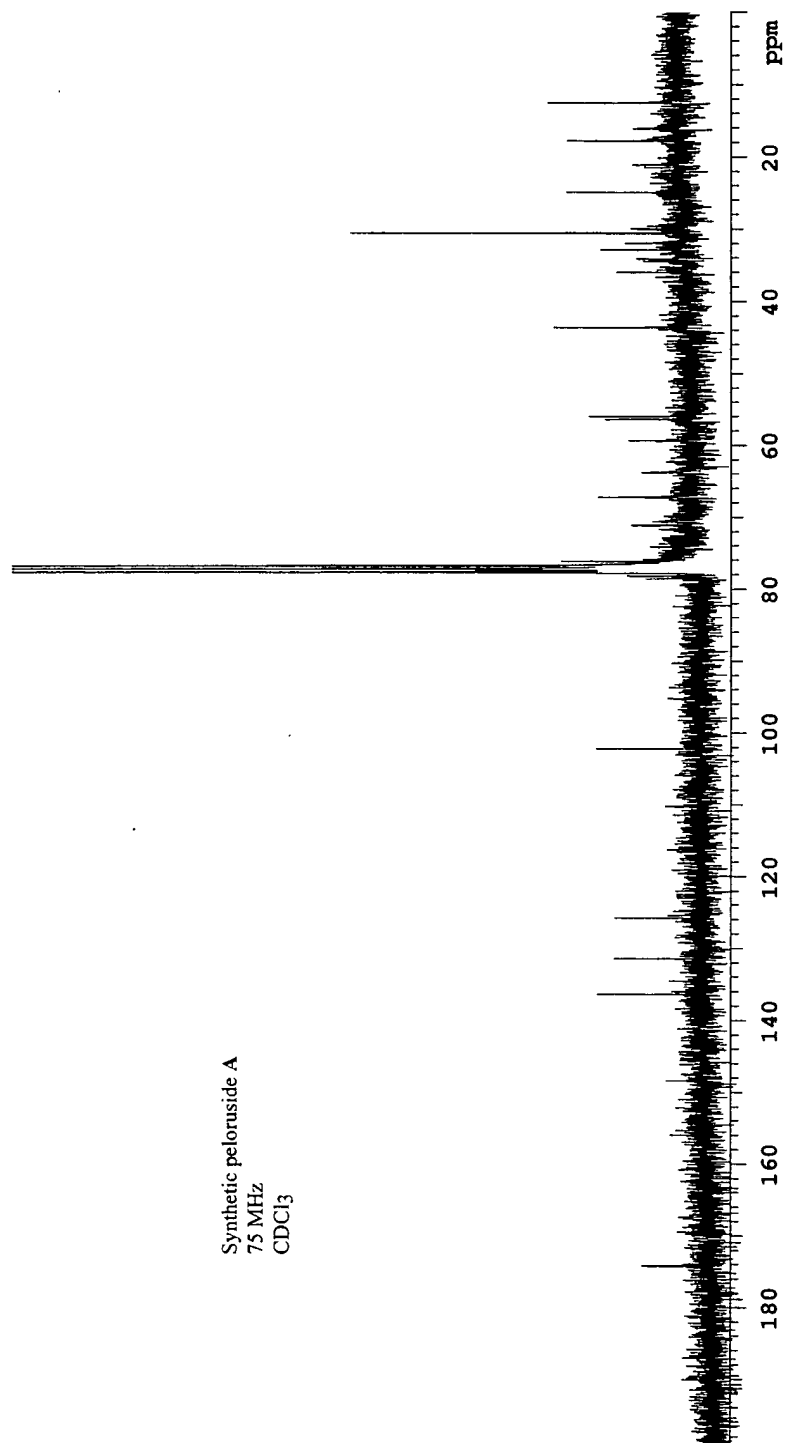


FIG. 4

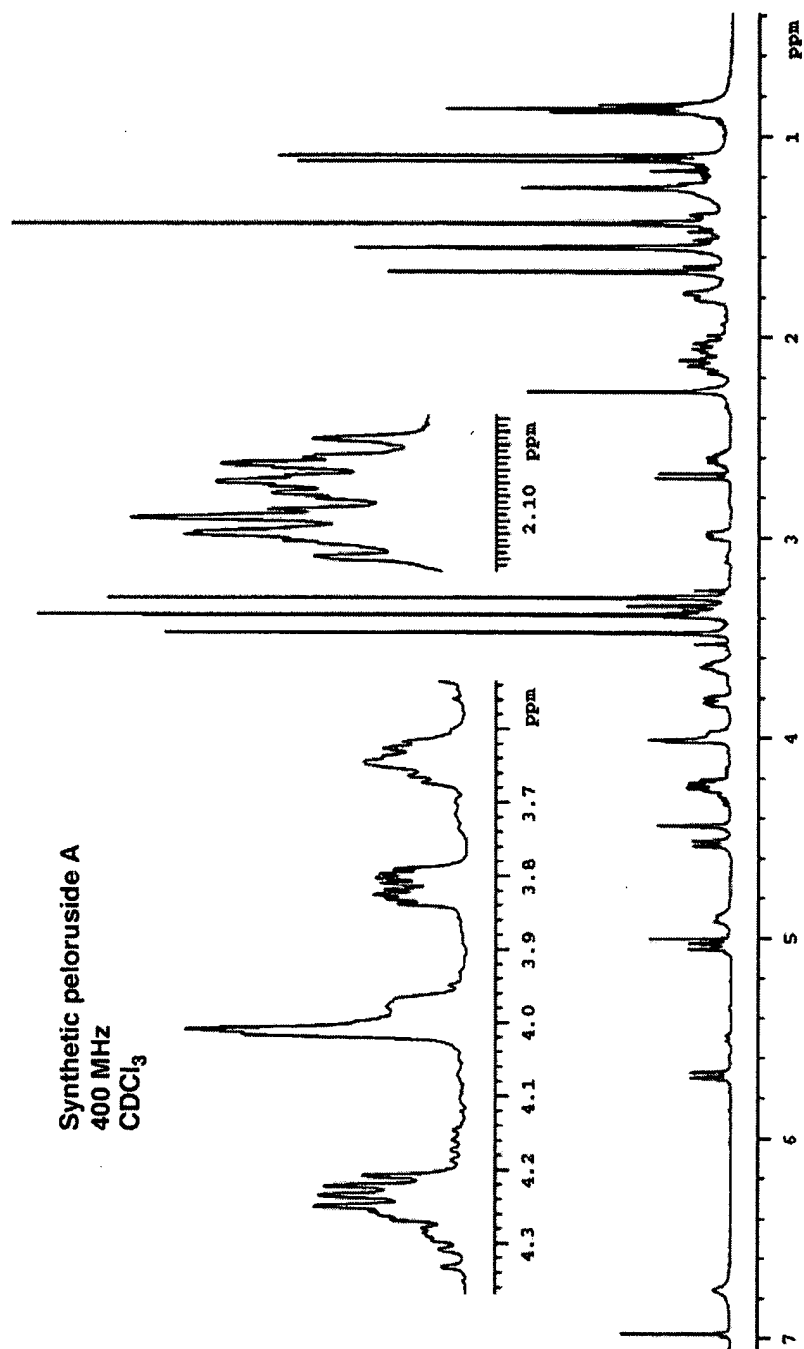


FIG. 5

C1-C13 Fragment:

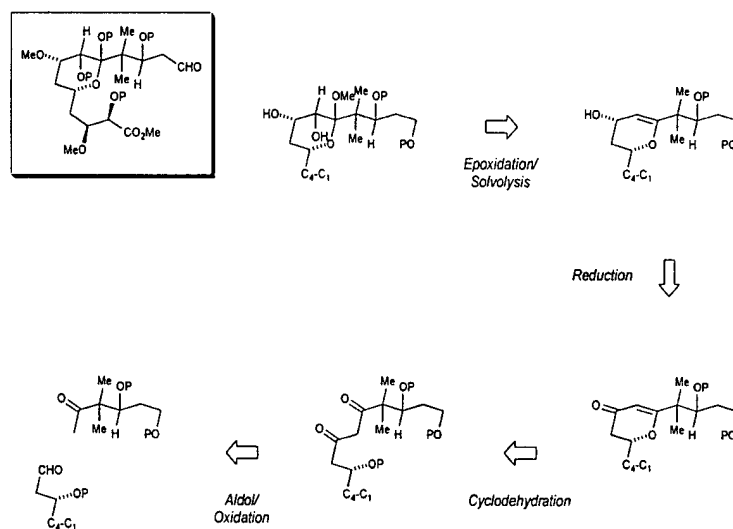


FIG. 6

C1-C13 Fragment: Problematic Glycal-Epoxyde Solvolysis

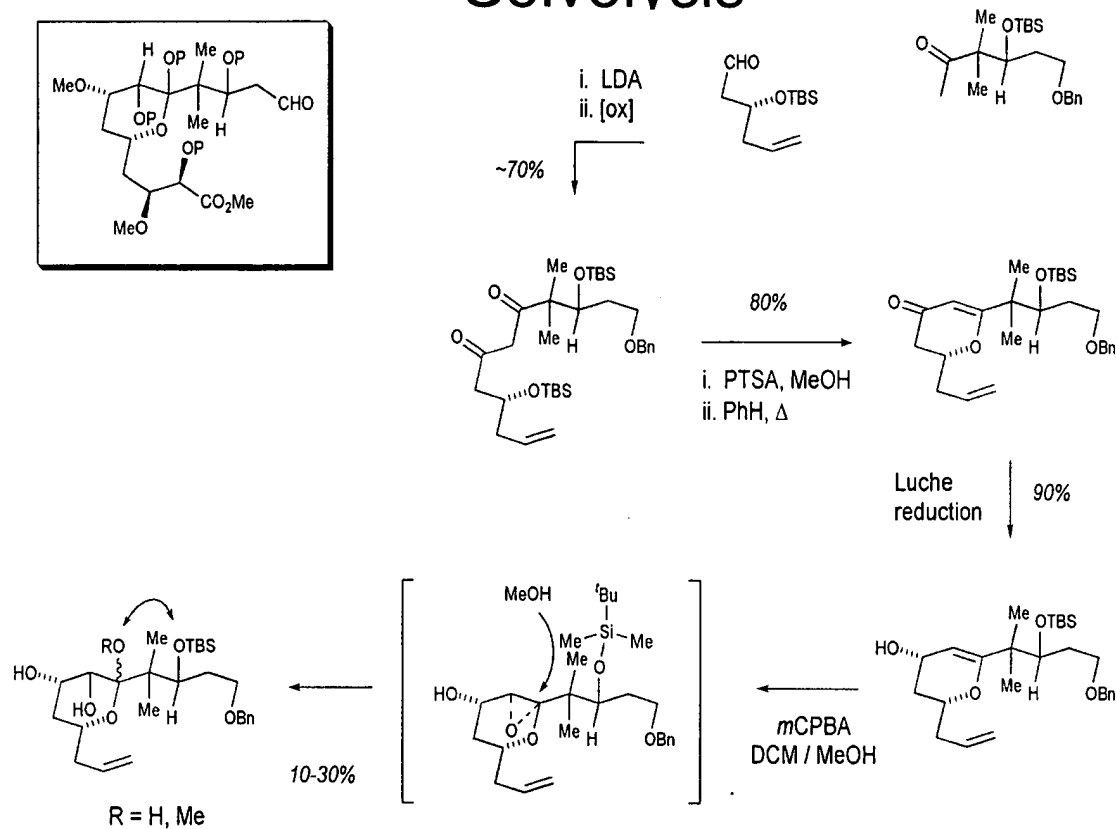


FIG. 7

Solution: Eliminate C11 Stereogenic Centrum

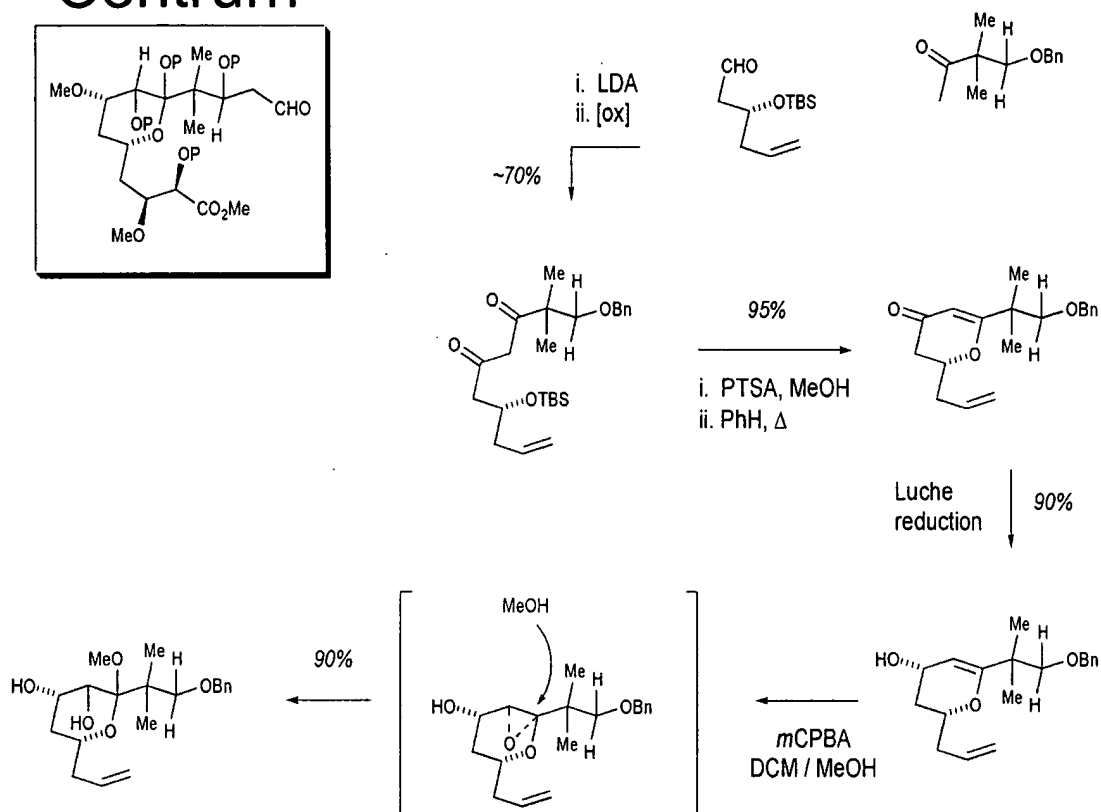


FIG. 8

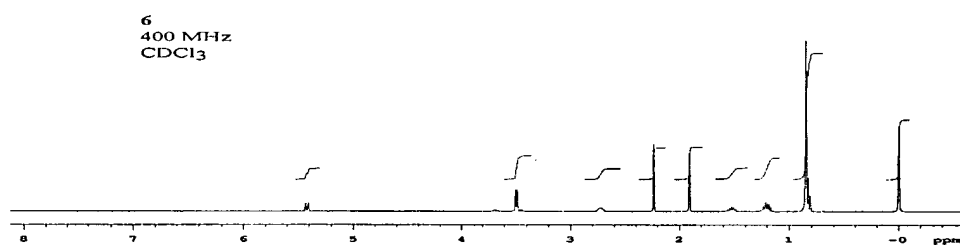


FIG. 9

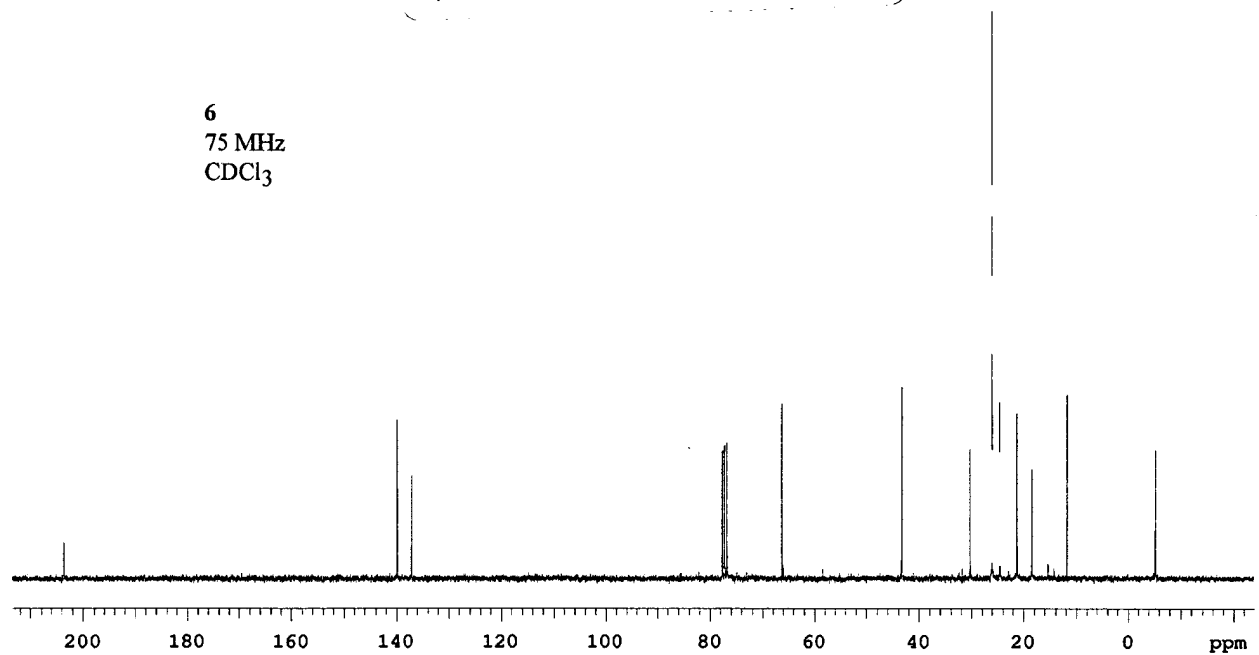


FIG. 10

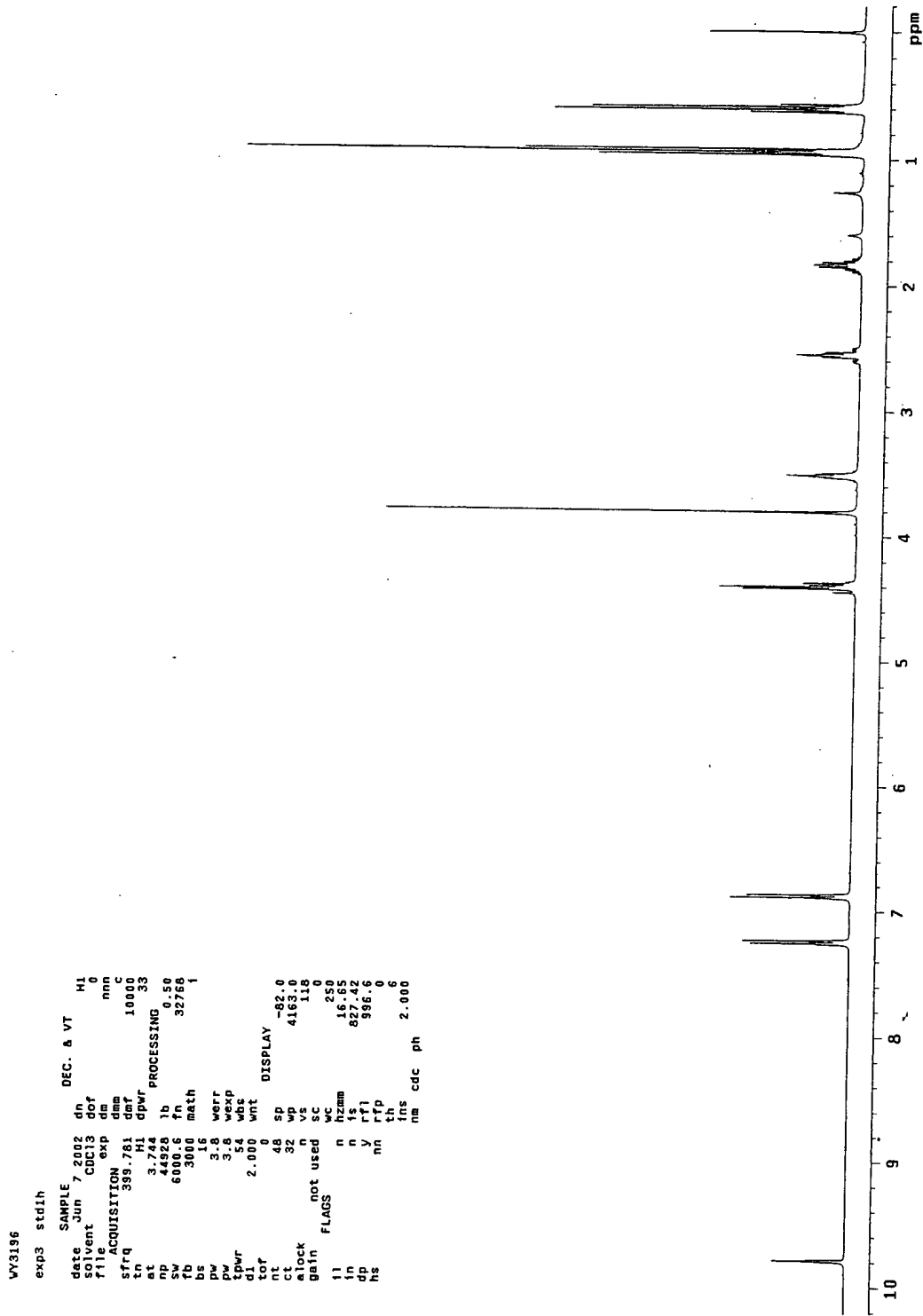


FIG. 11

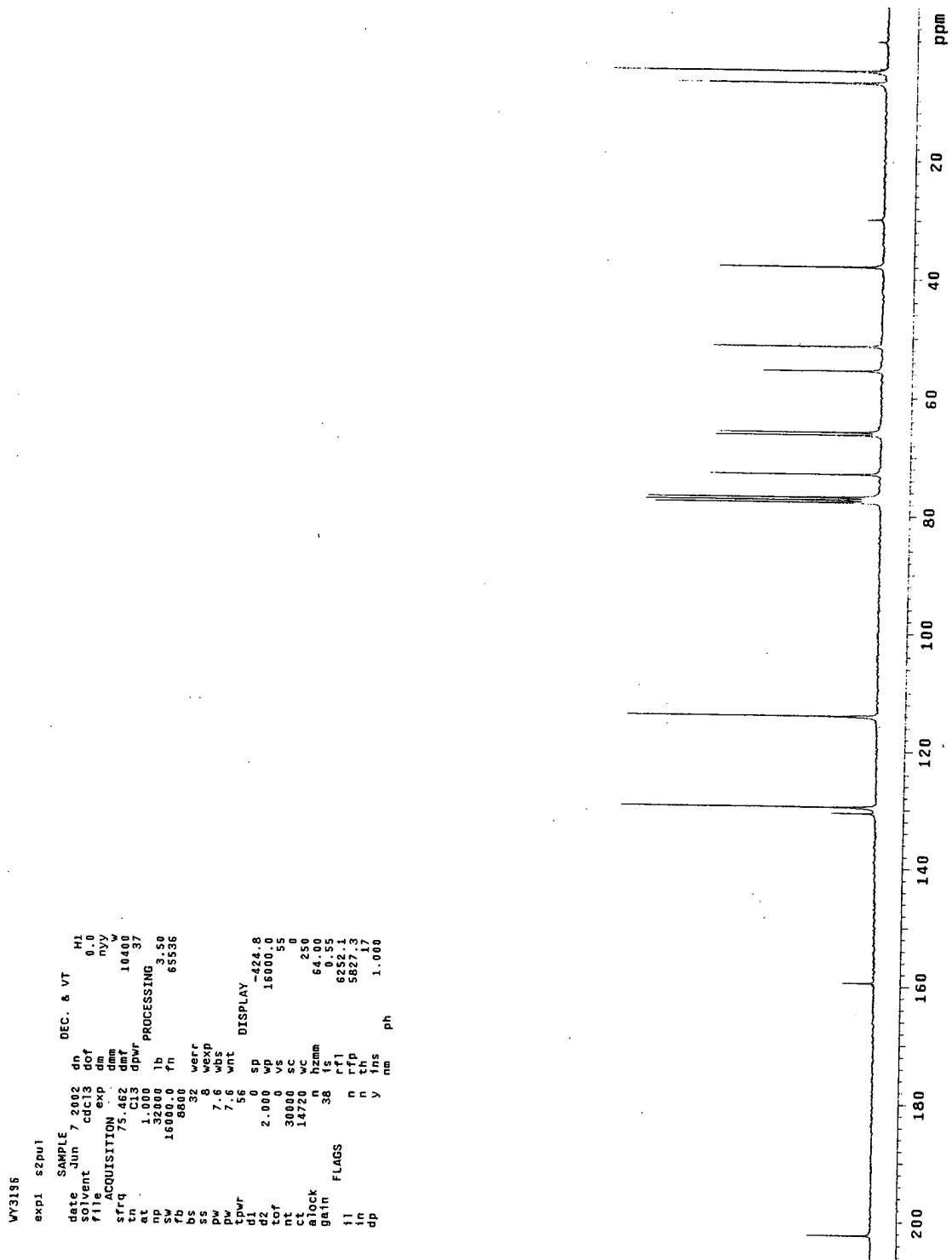


FIG. 12

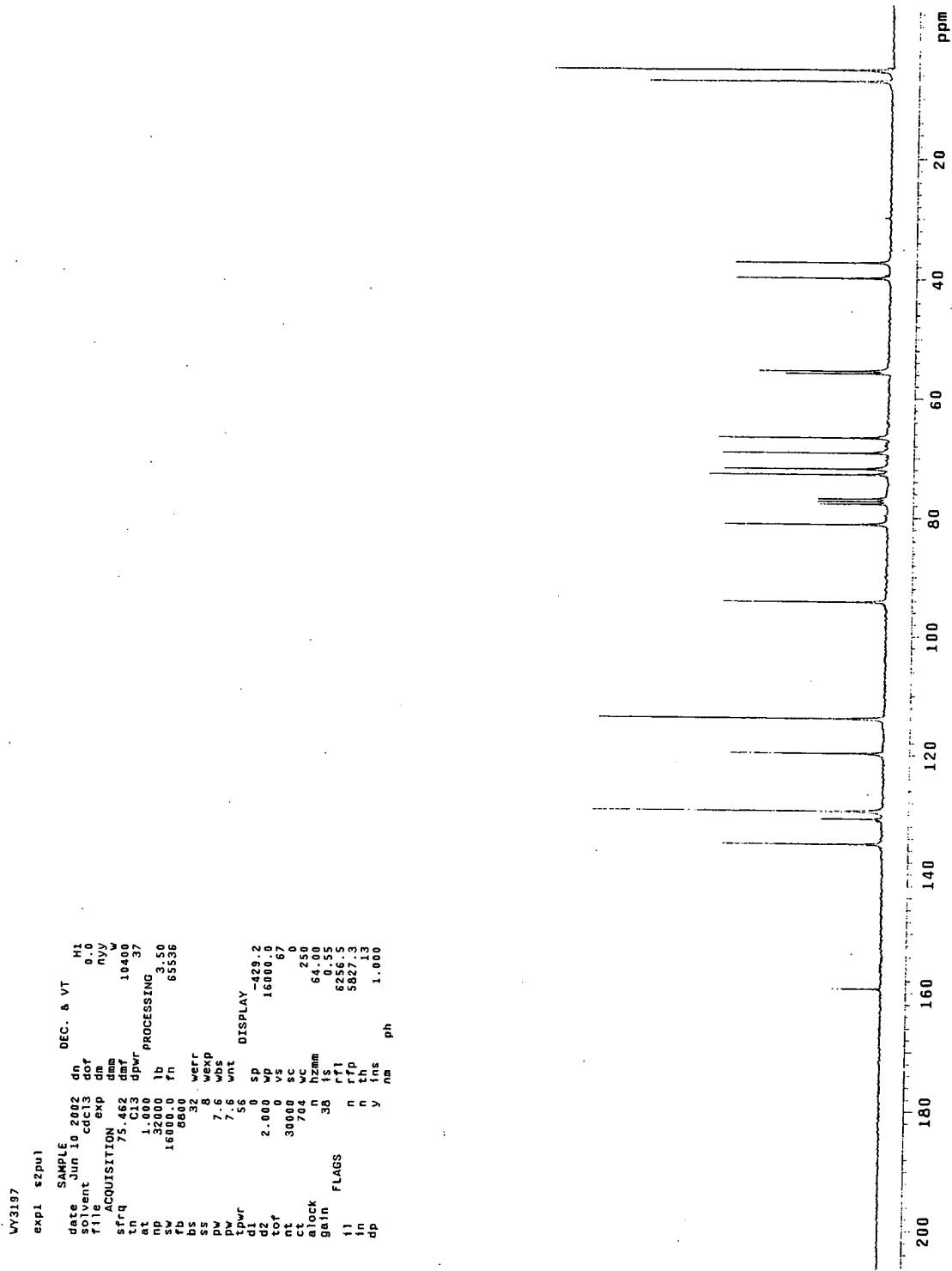


FIG. 14

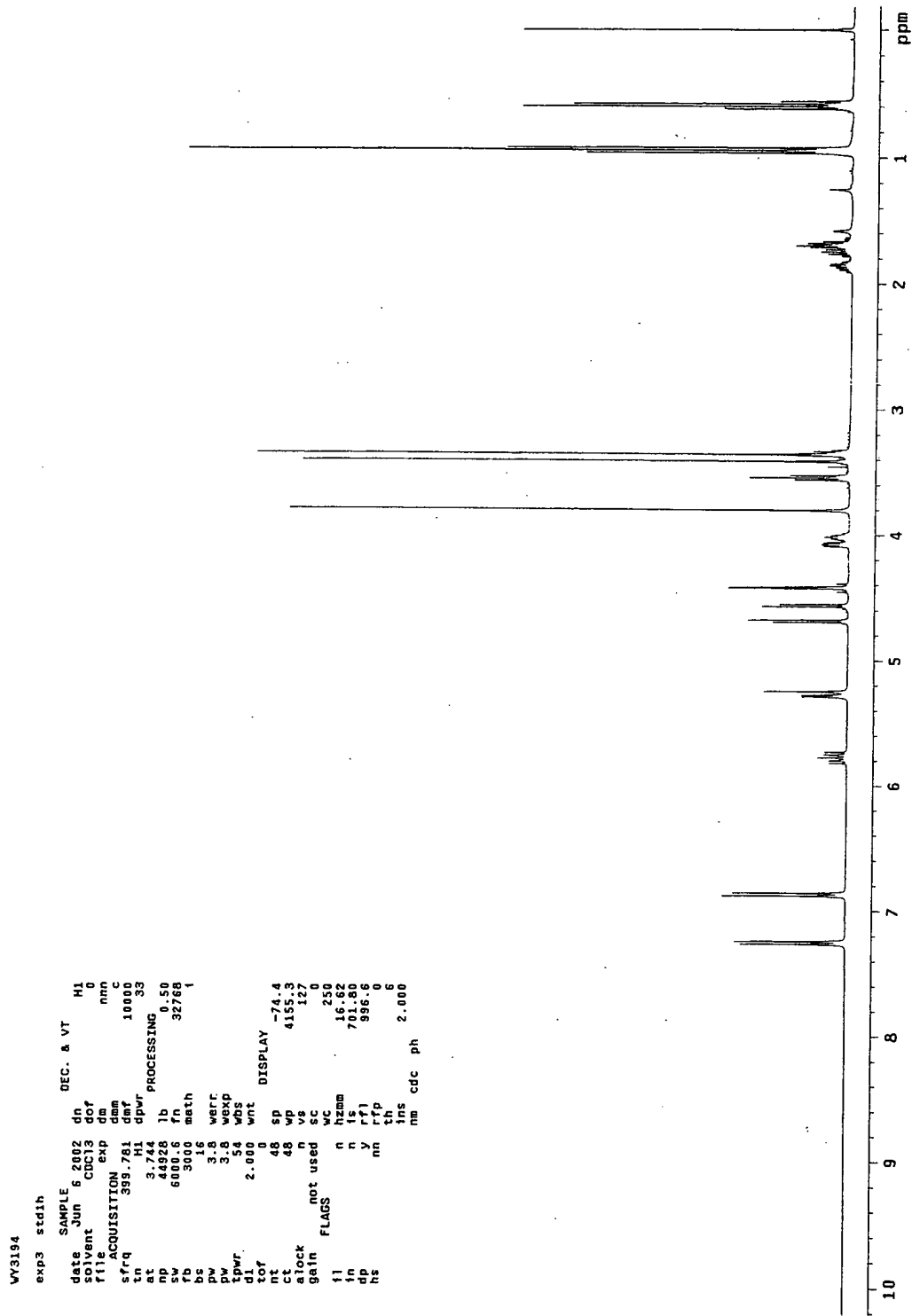


FIG. 15

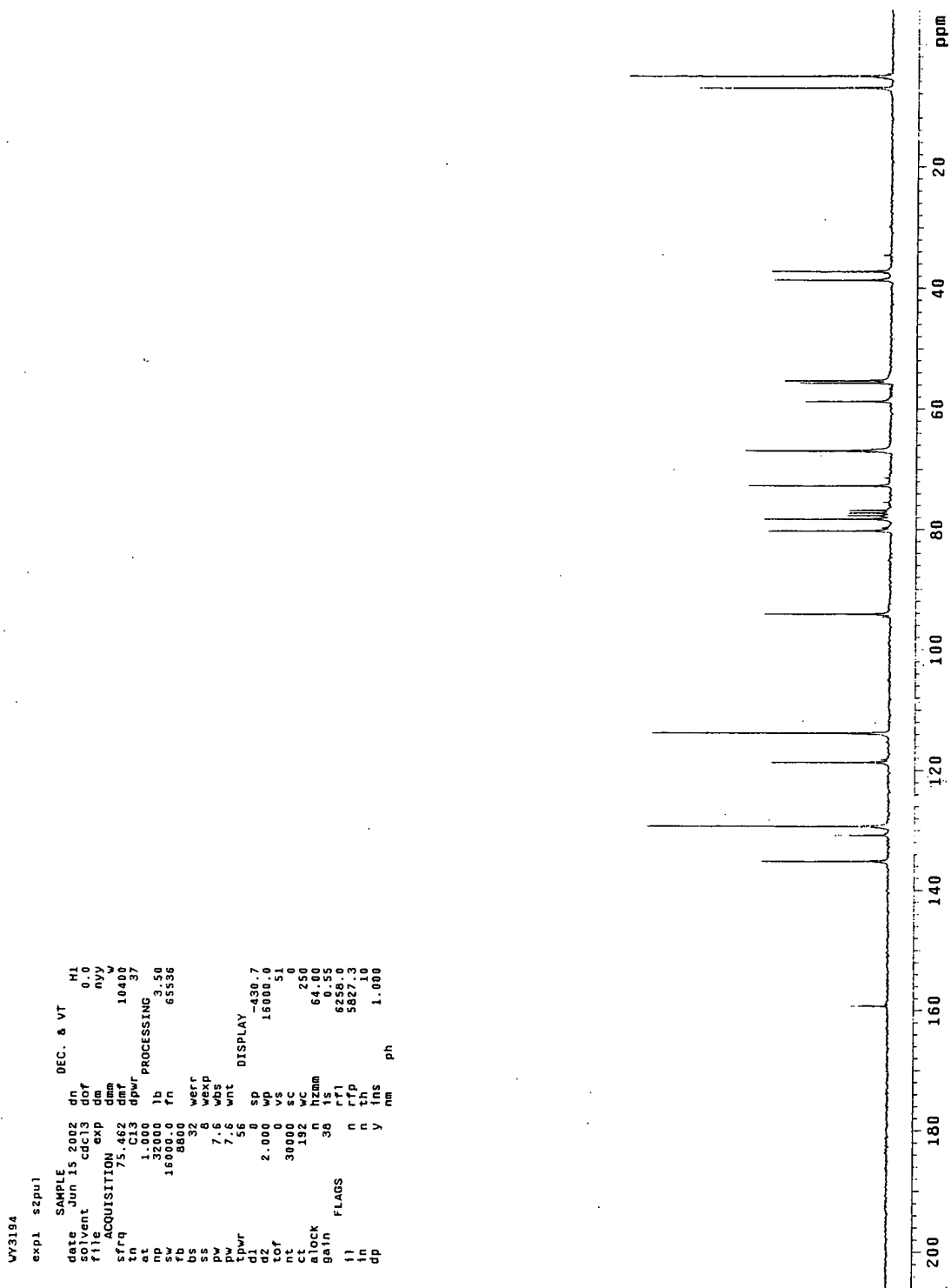


FIG. 16

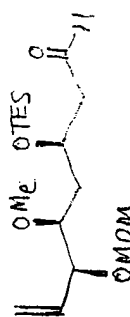
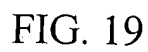


FIG. 17



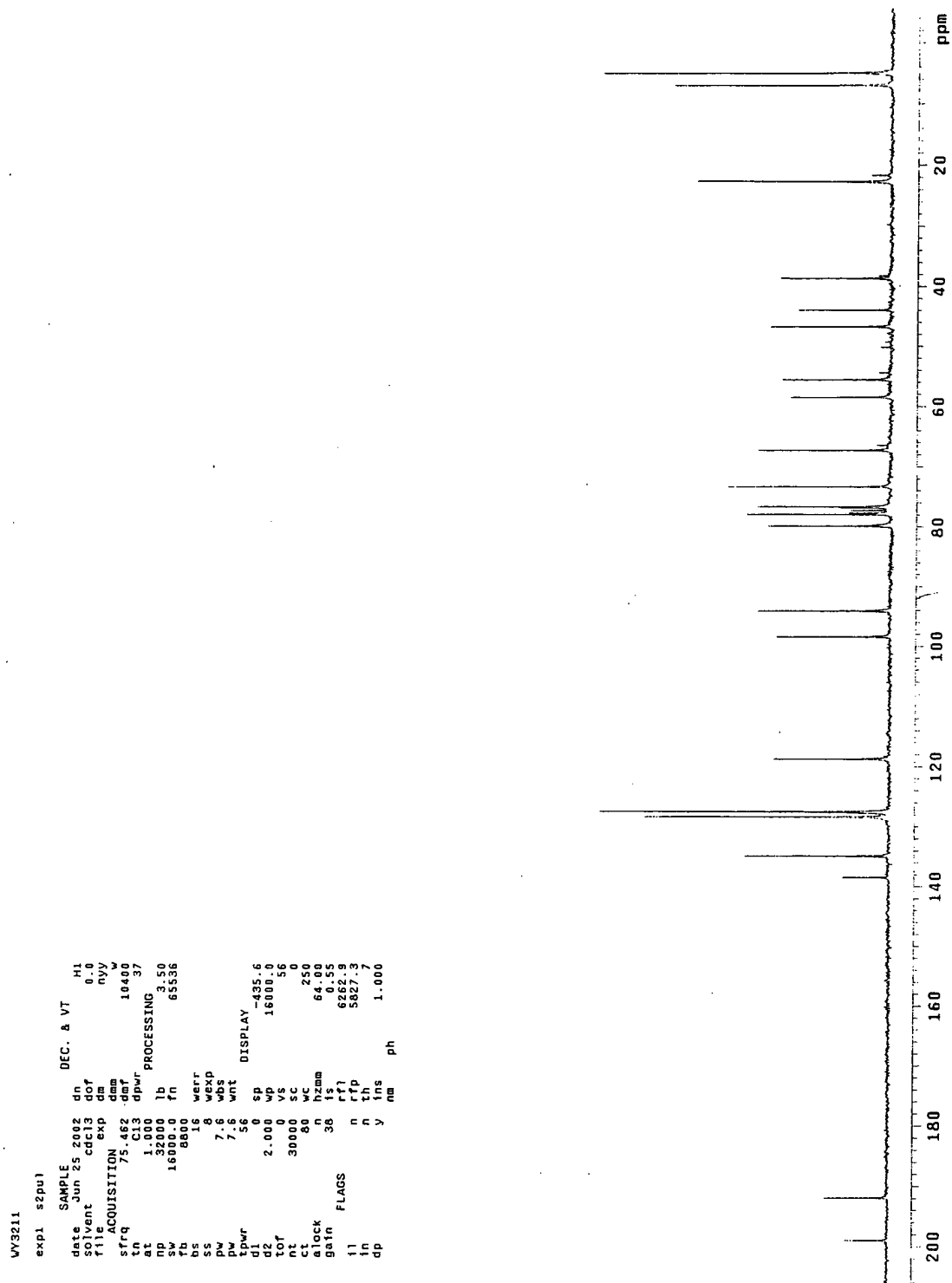


FIG. 20

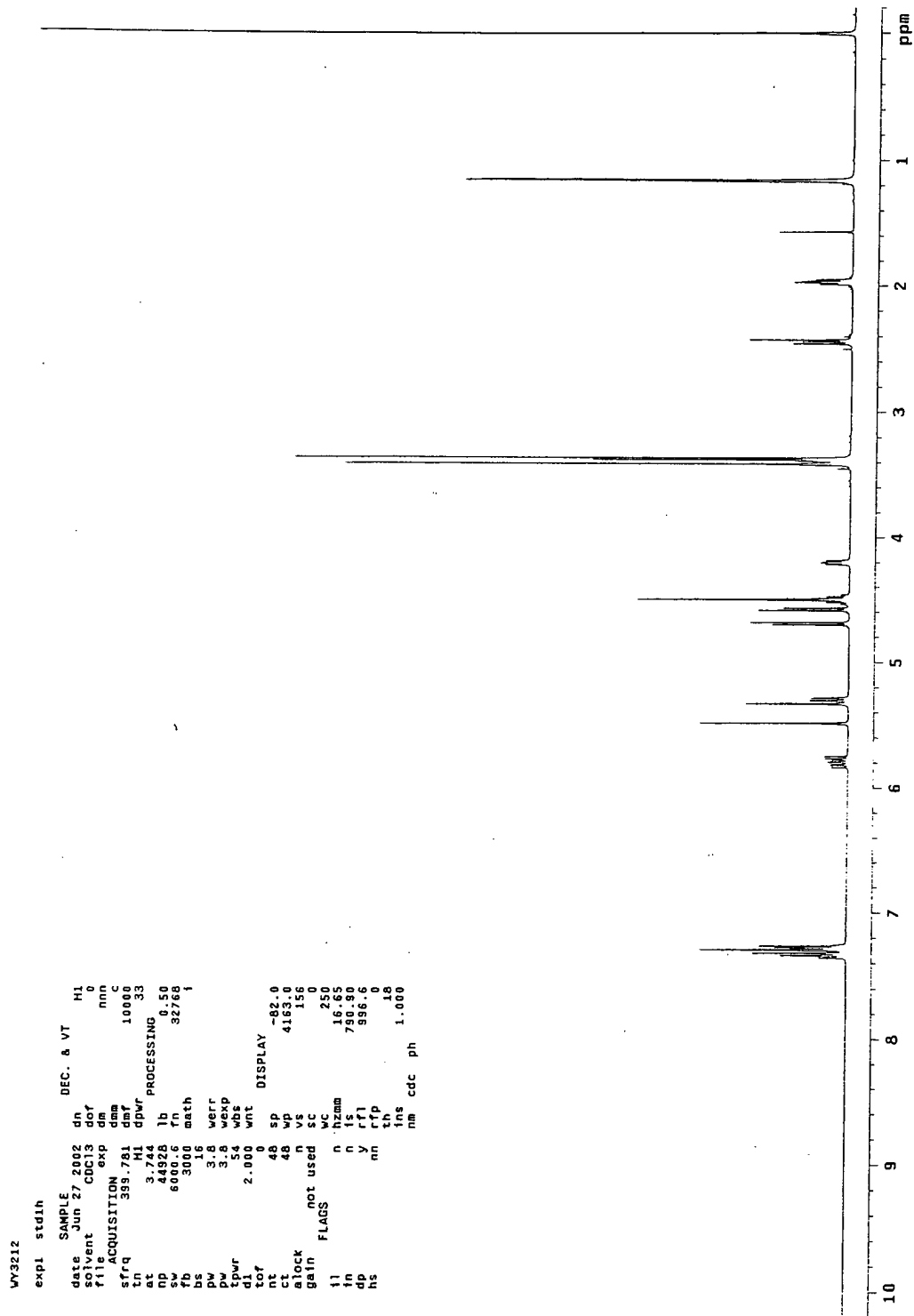


FIG. 21

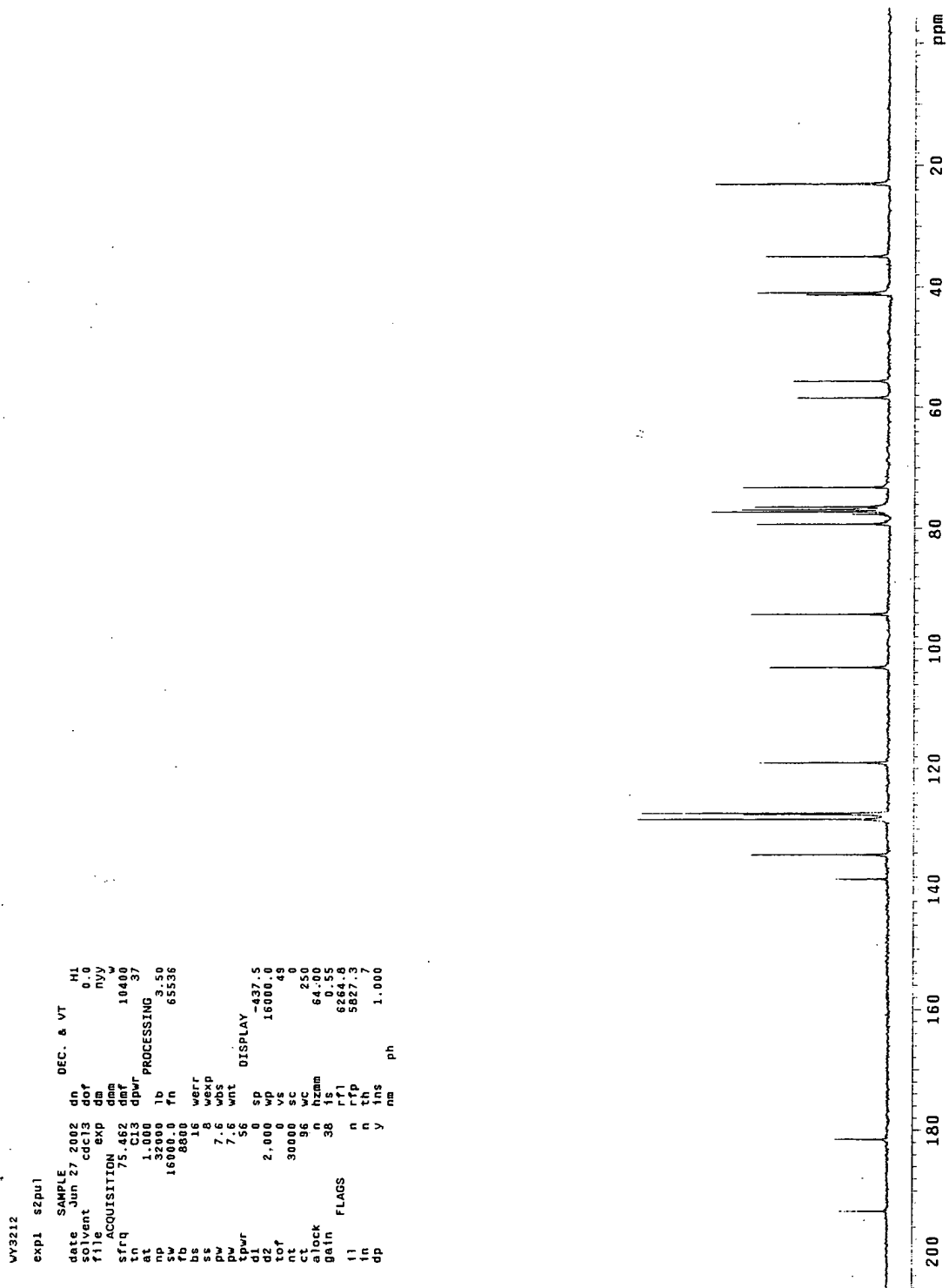


FIG. 22

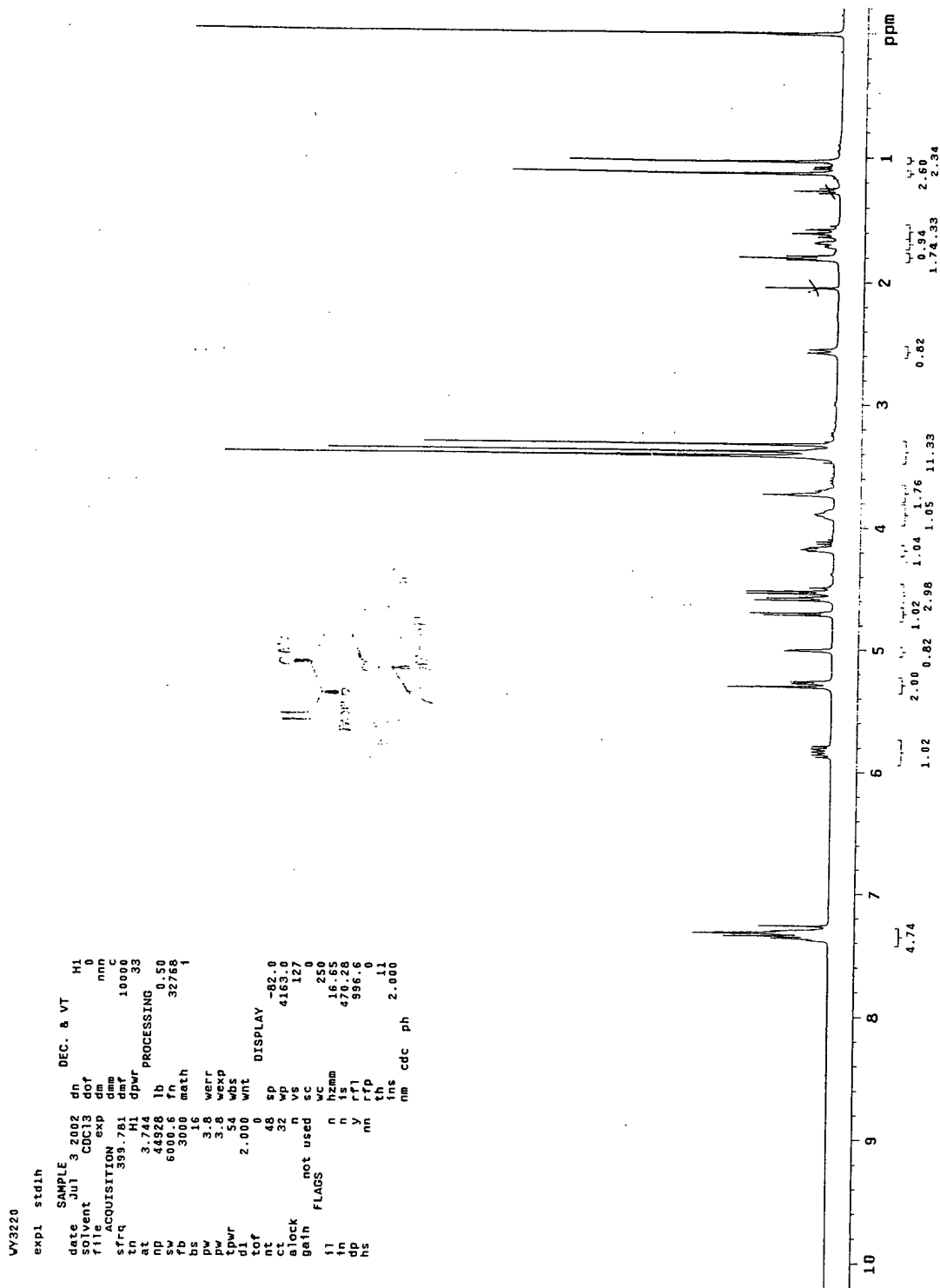


FIG. 23

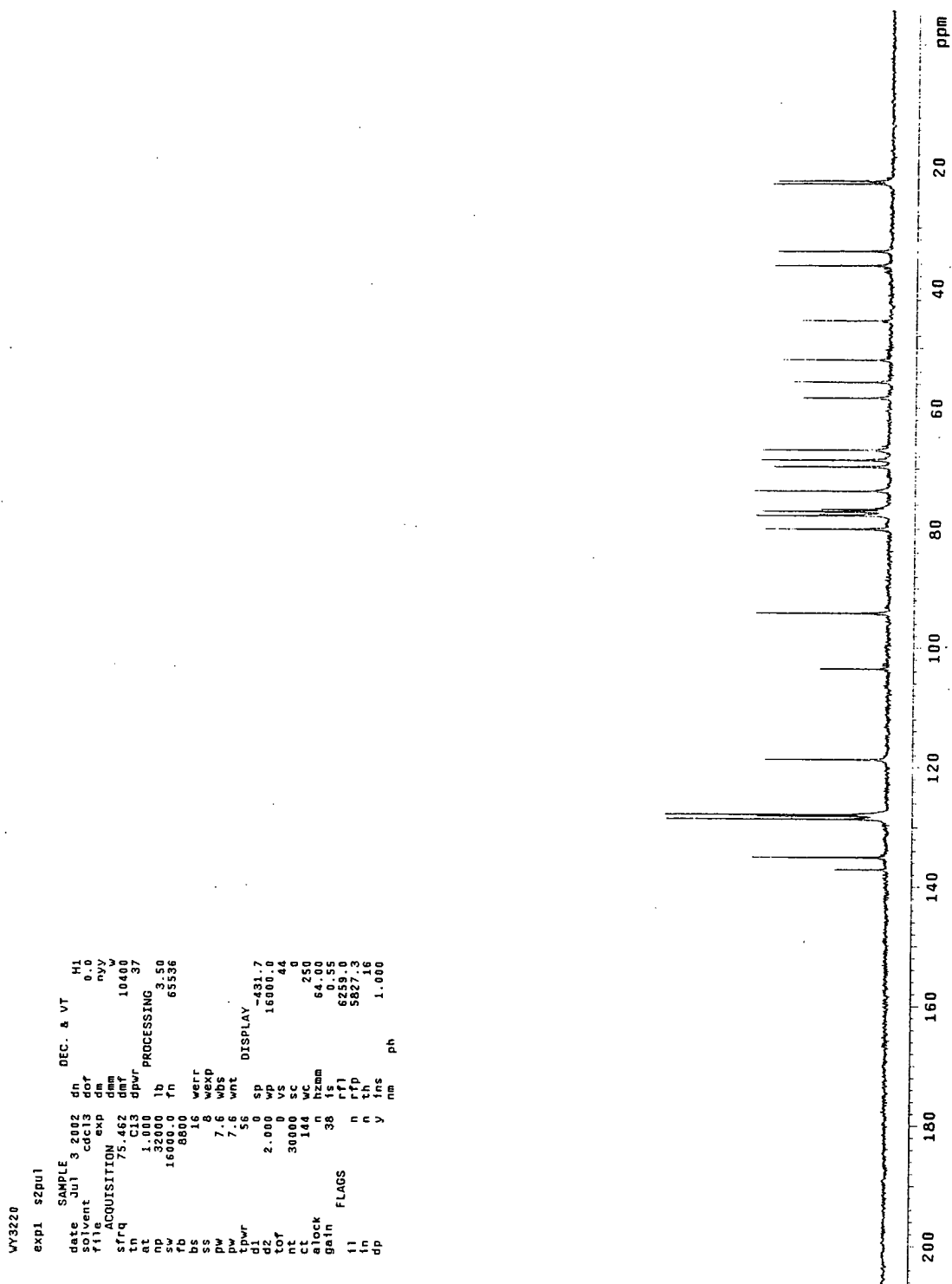


FIG. 24

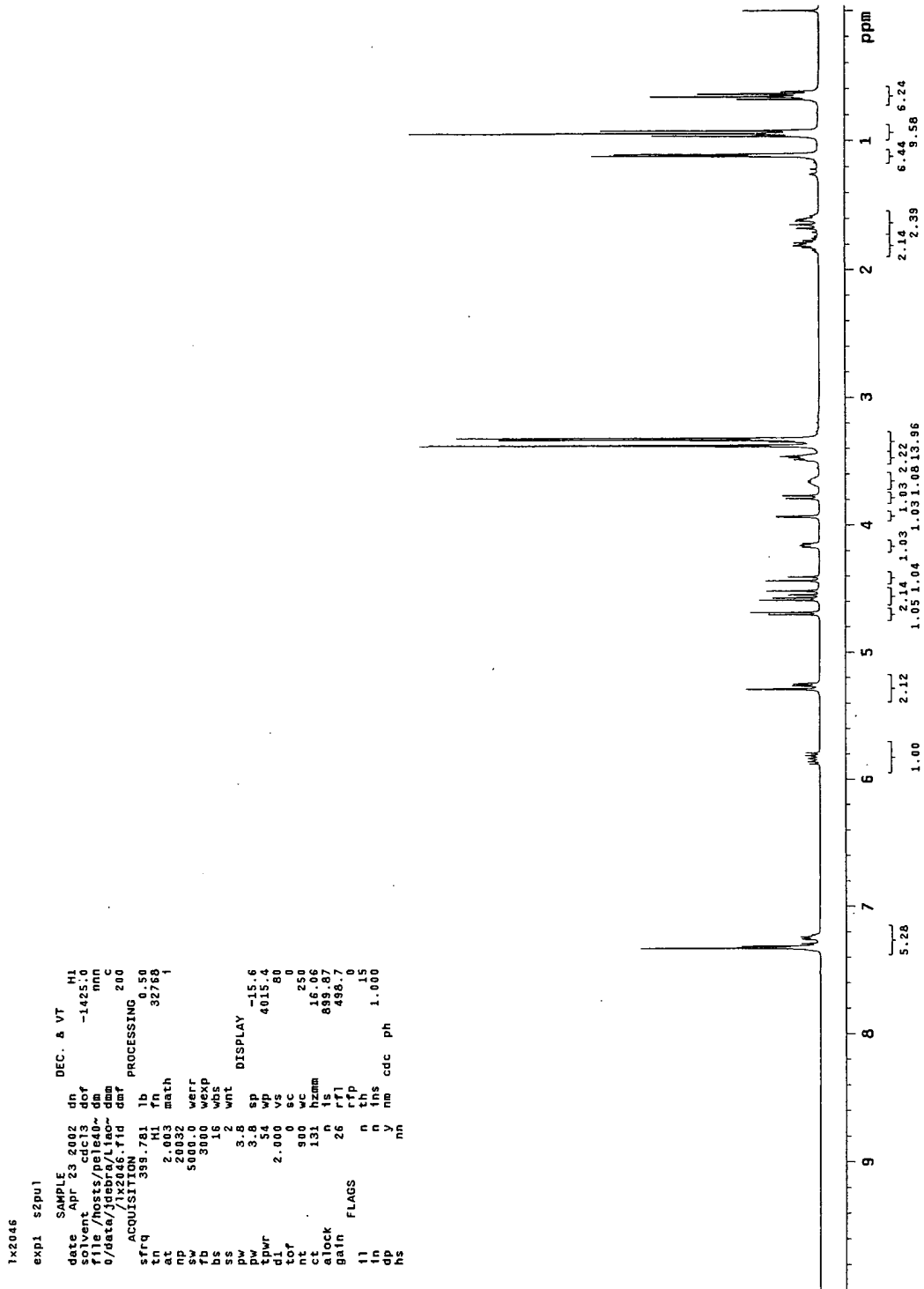


FIG. 25

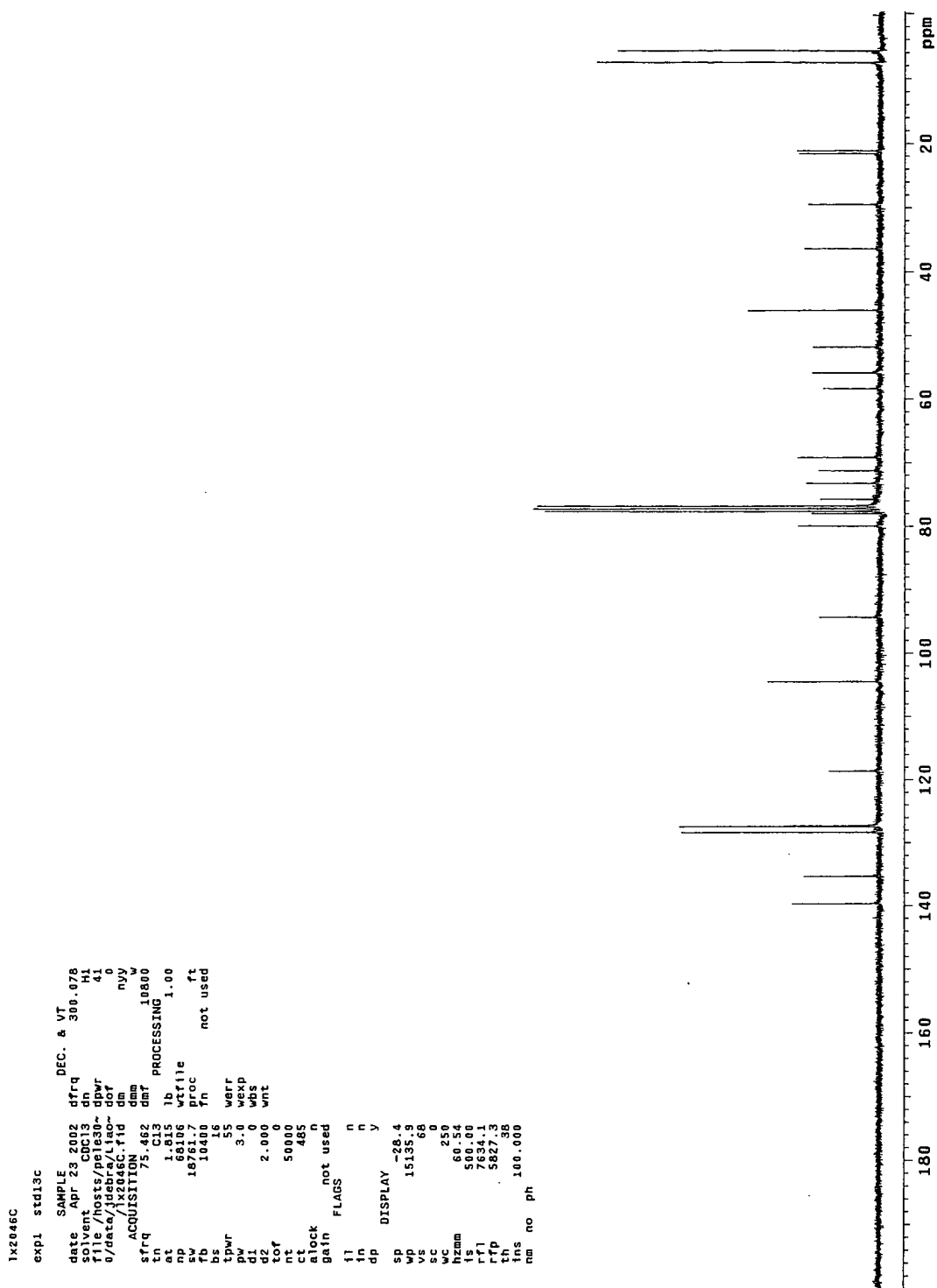
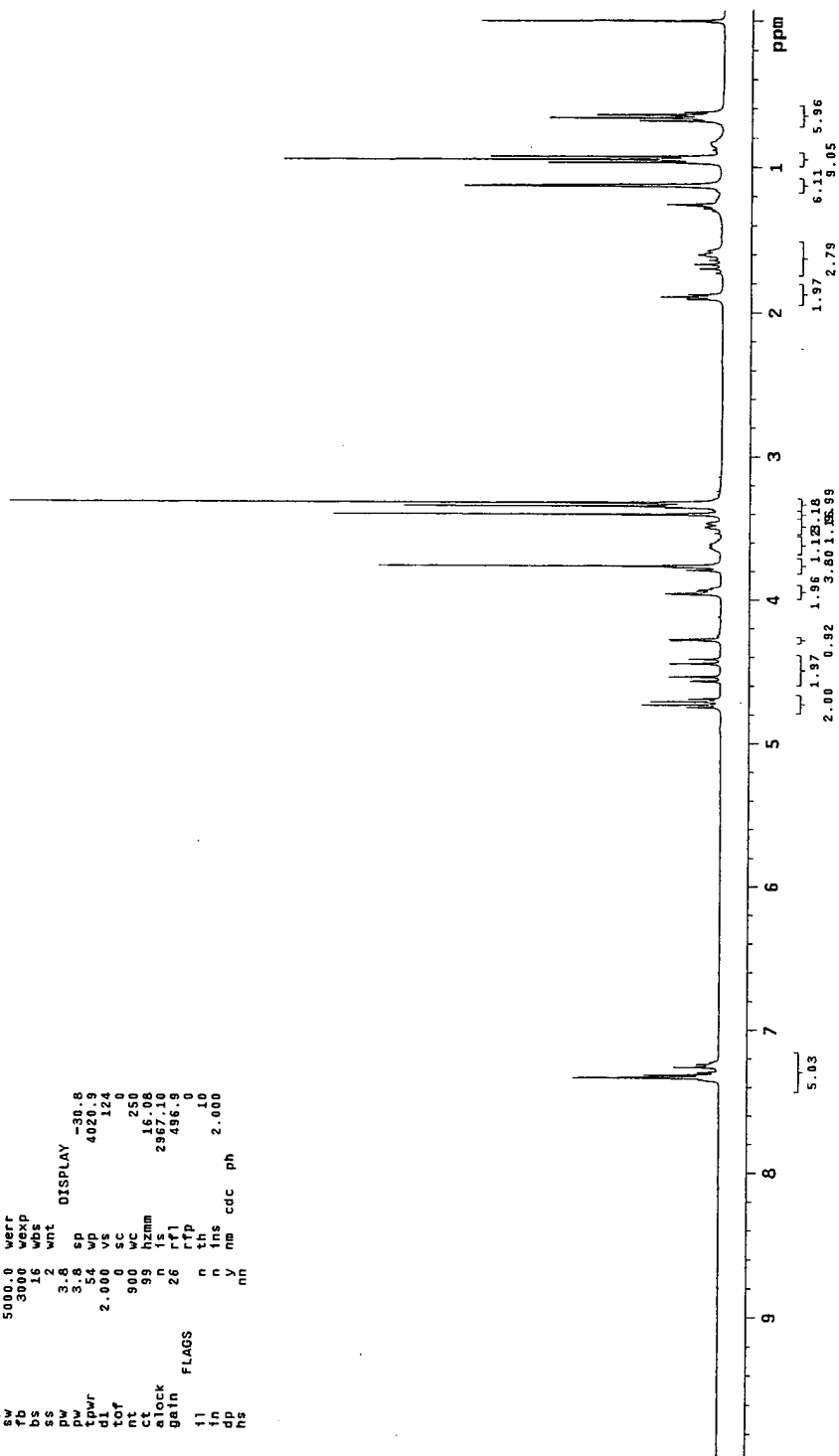


FIG. 26



14

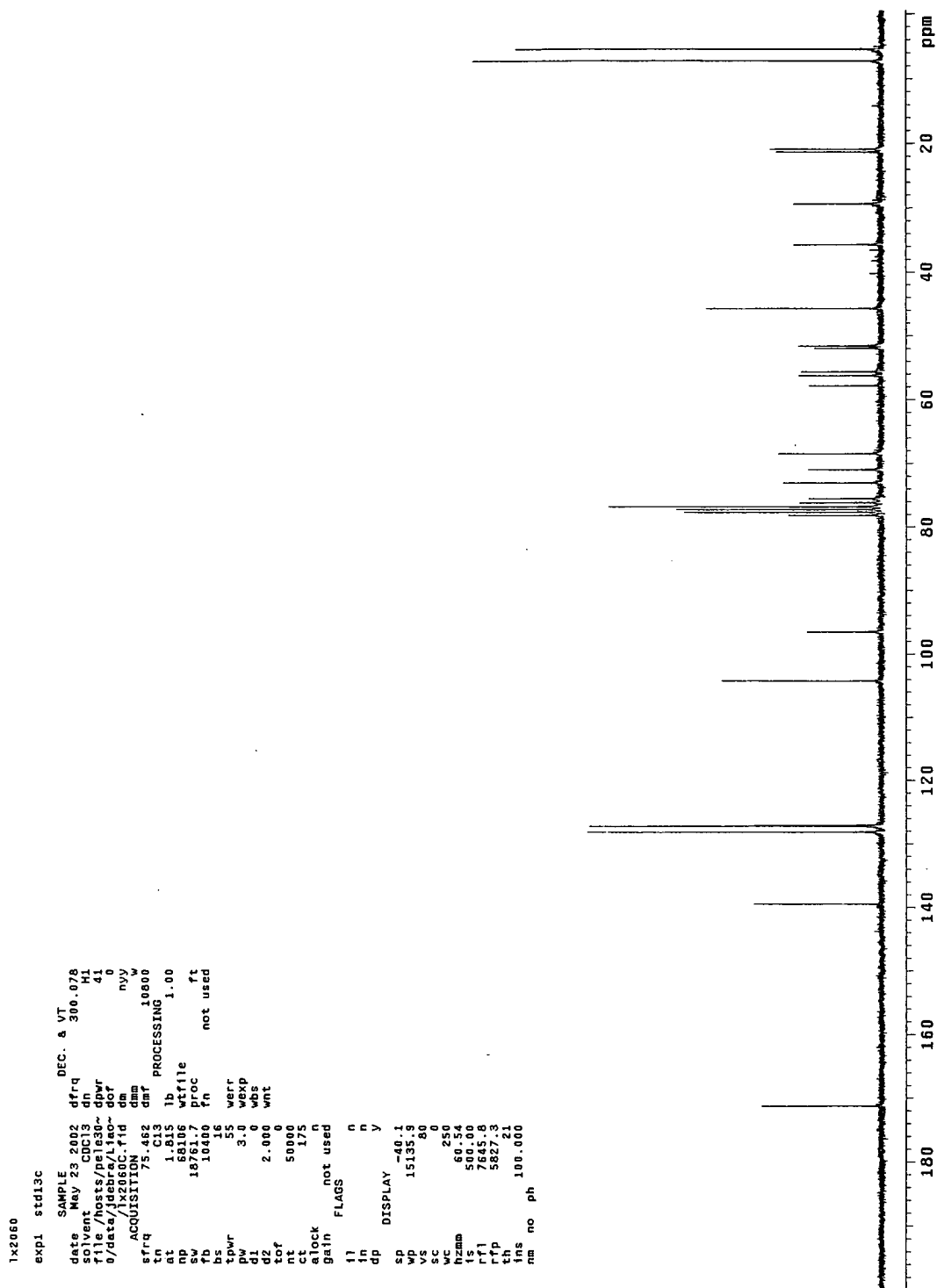


FIG. 28

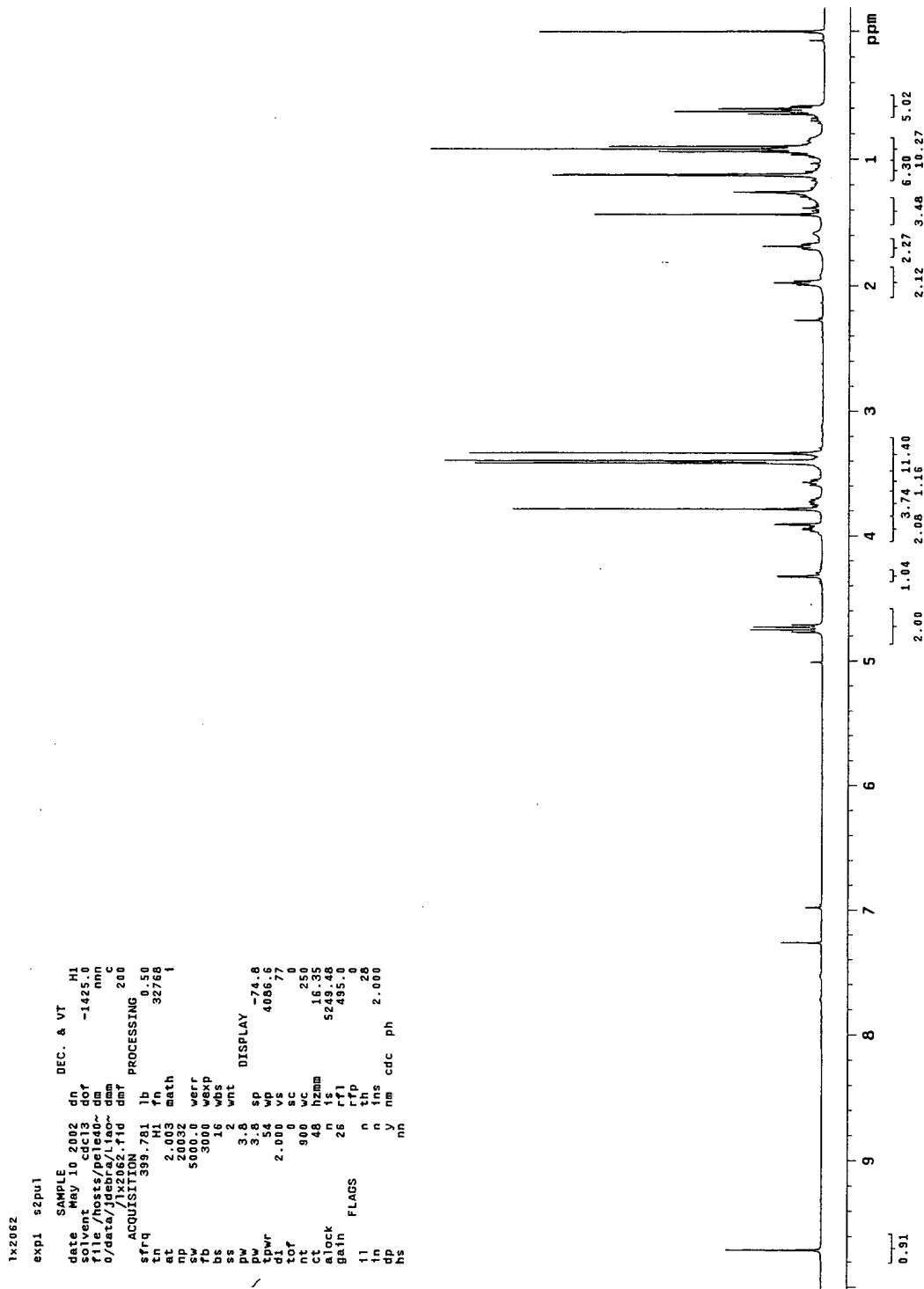


FIG.29

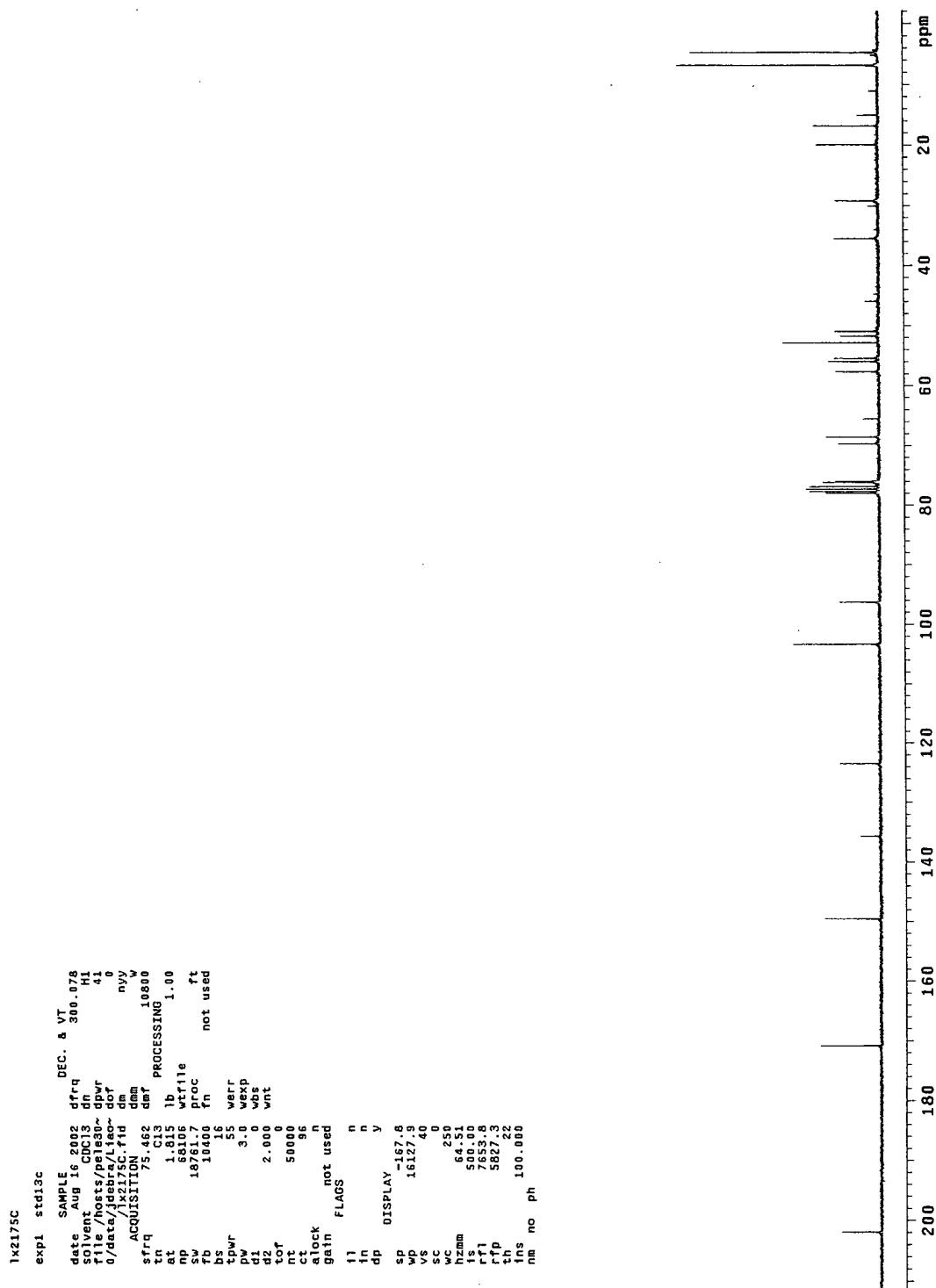


FIG. 30

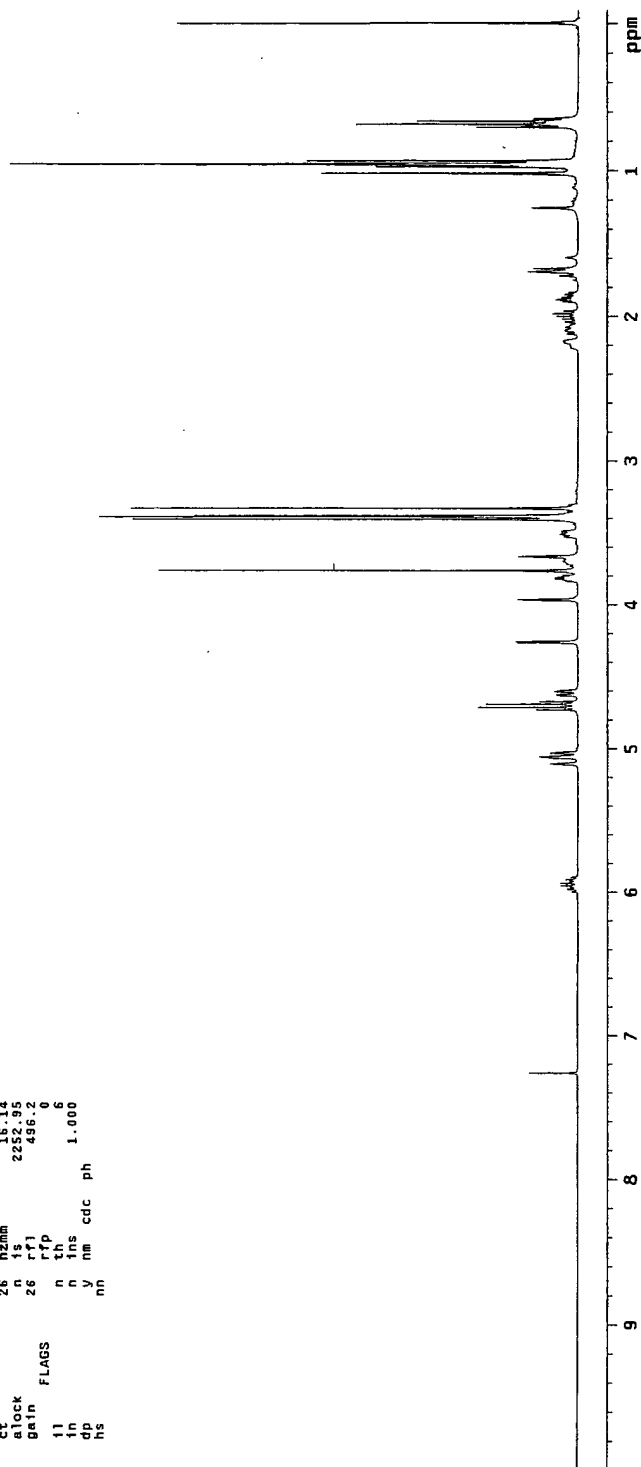


FIG. 31

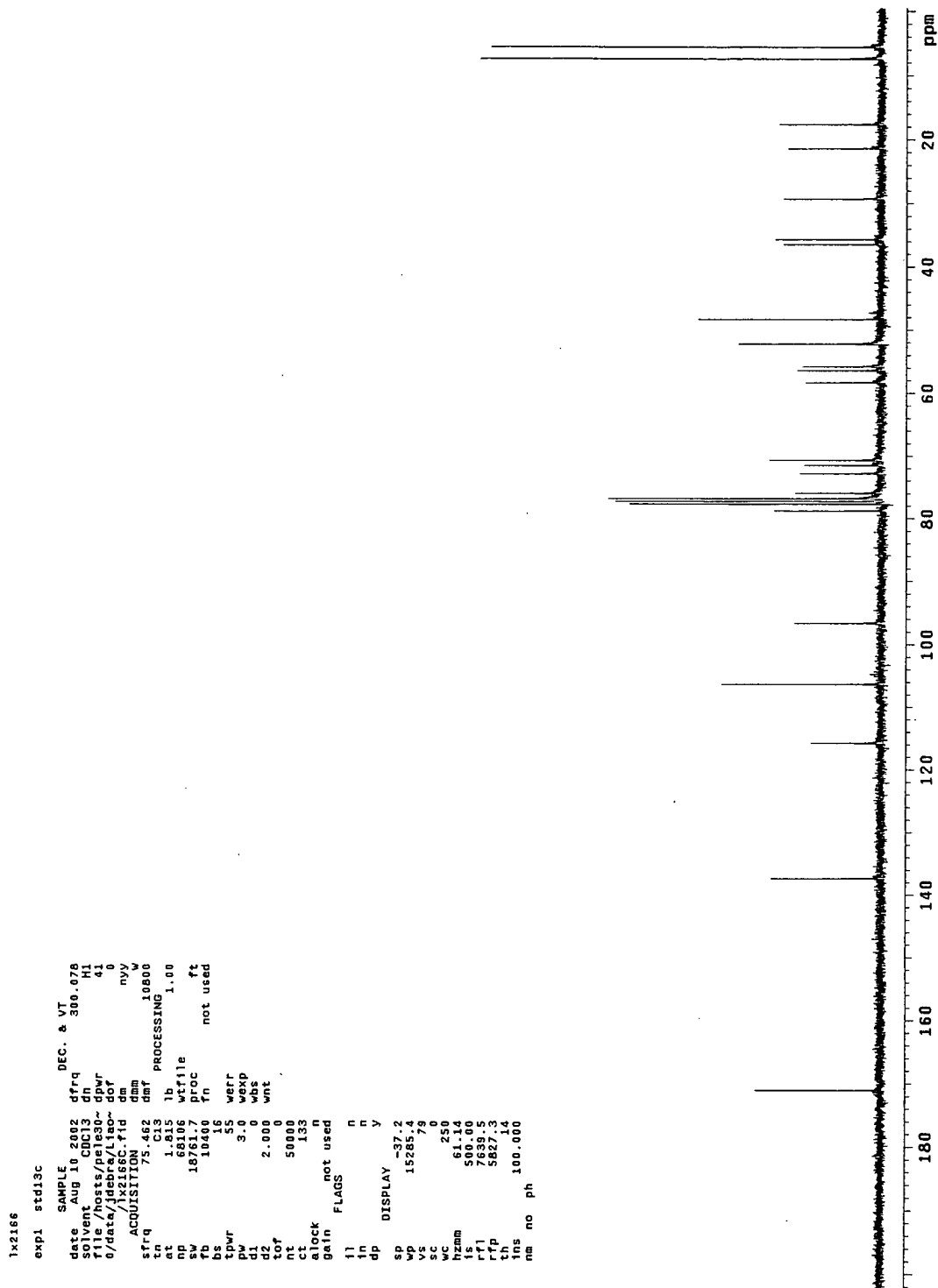


FIG. 32

24
400 MHz
CDCl₃

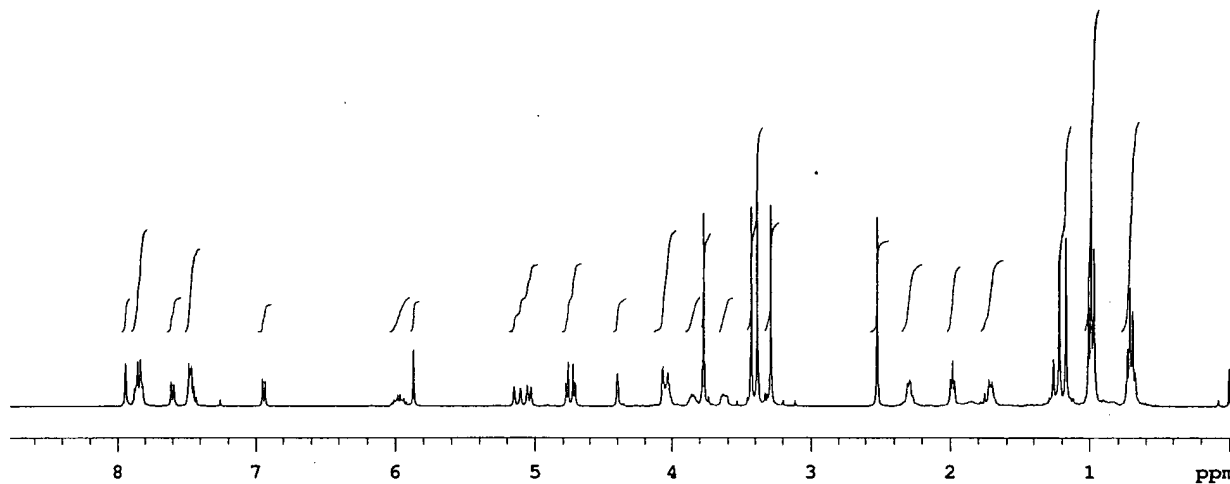


FIG. 33

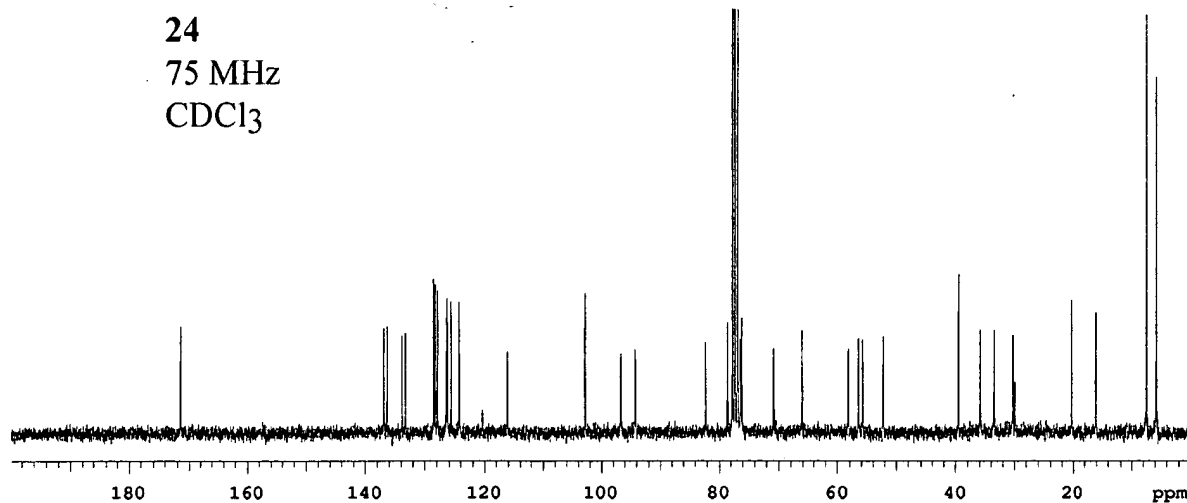


FIG. 34

24 1D-NOE Irradiation at 5.87 ppm
400 MHz
CDCl₃

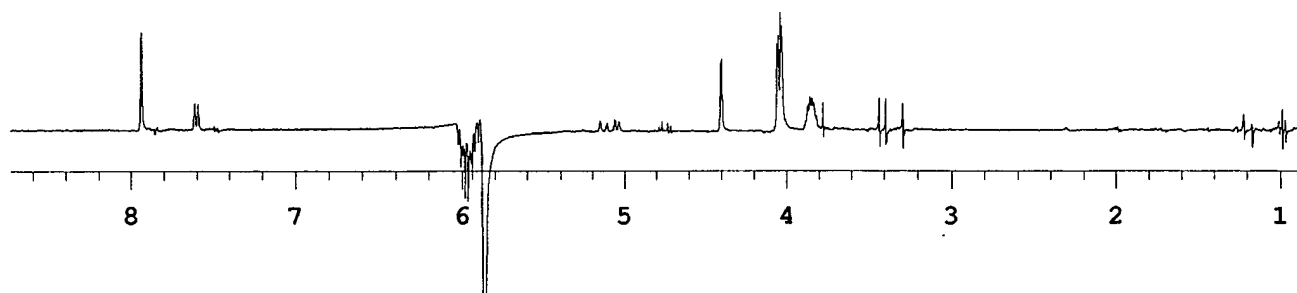


FIG. 35

24 1D-NOE Irradiation at 1.22 ppm
400 MHz
CDCl₃

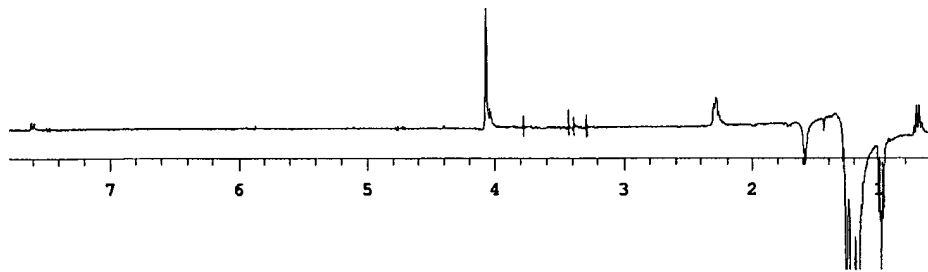


FIG. 36

29
400 MHz
CDCl₃

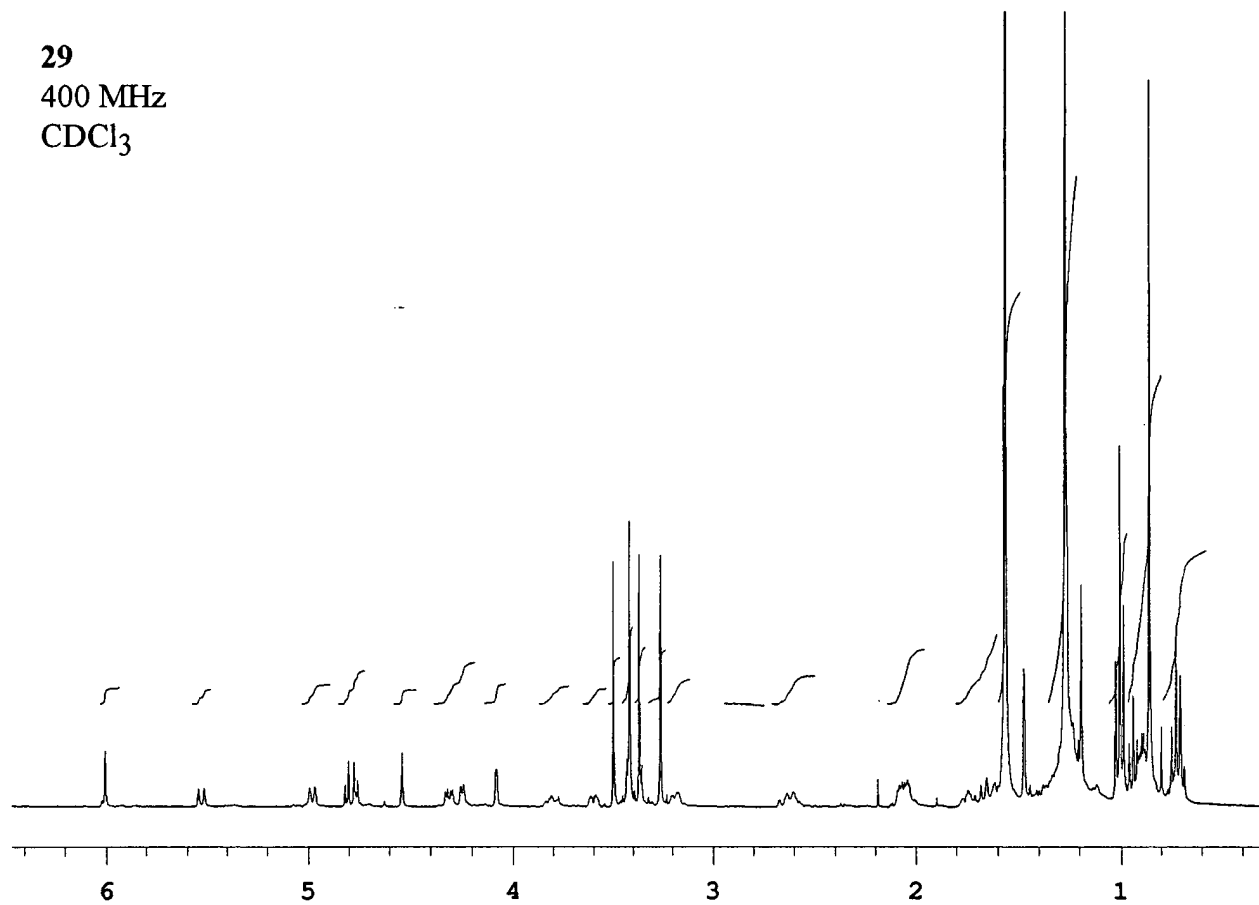


FIG. 37

29 1D-NOE Irradiation at 5.53 ppm
400 MHz
CDCl₃

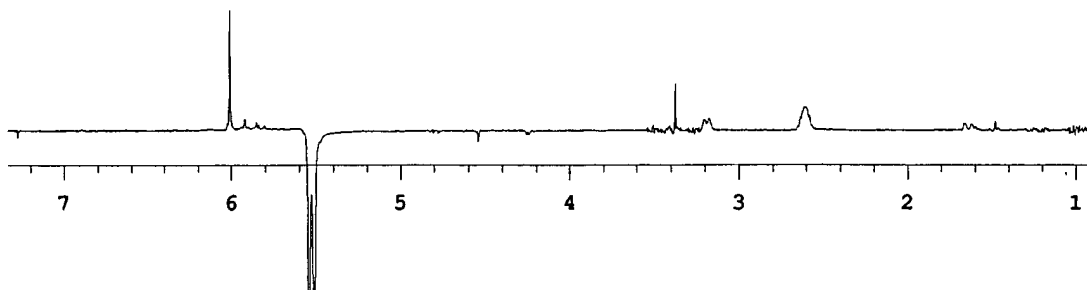


FIG. 38

²⁹ 1D-NOE Irradiation at 4.54 ppm

400 MHz

CDCl₃

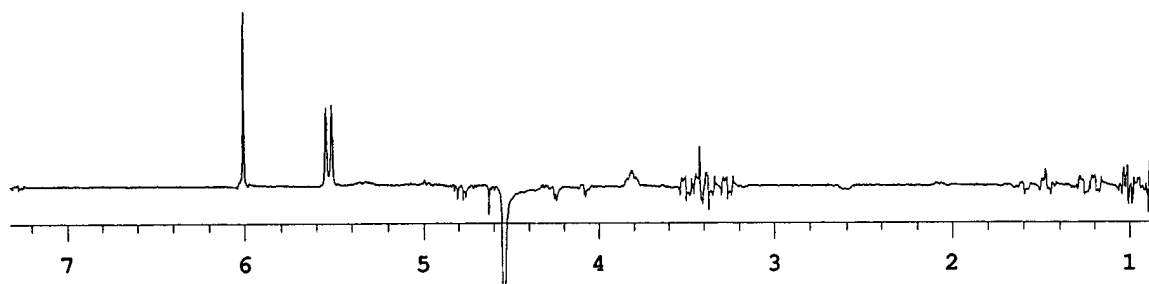


FIG. 39

Compound 29 2D NOE
400MHz CDCl₃

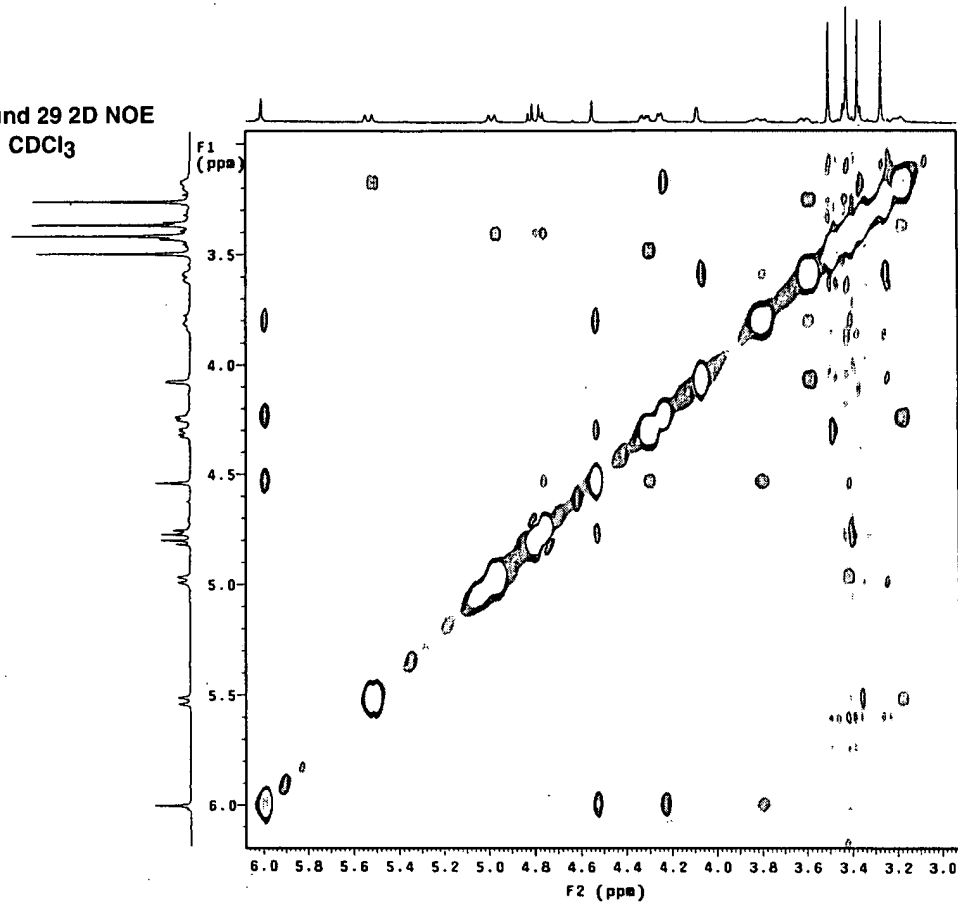


FIG. 40

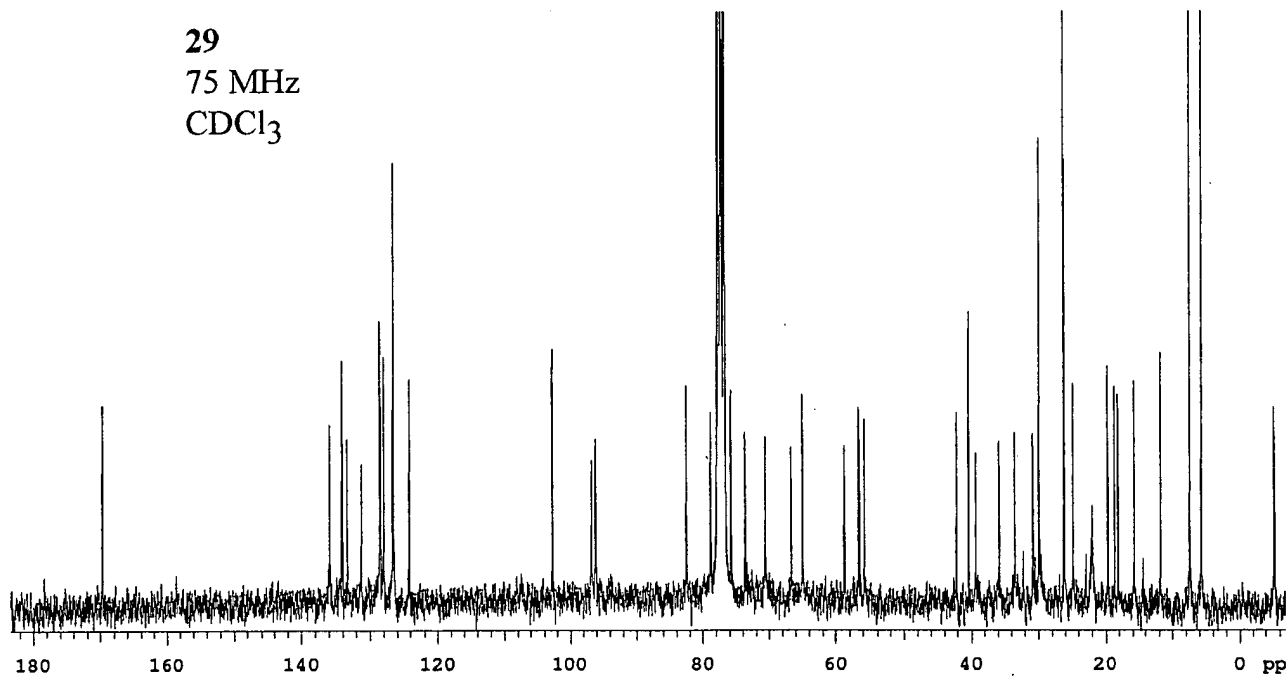


FIG. 41

30
400 MHz
CDCl₃

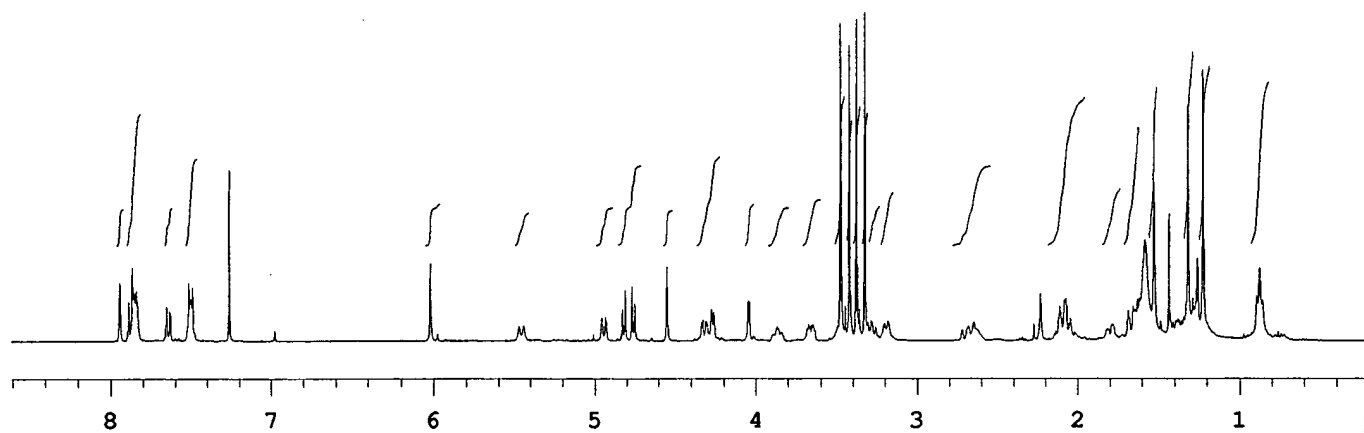


FIG. 42

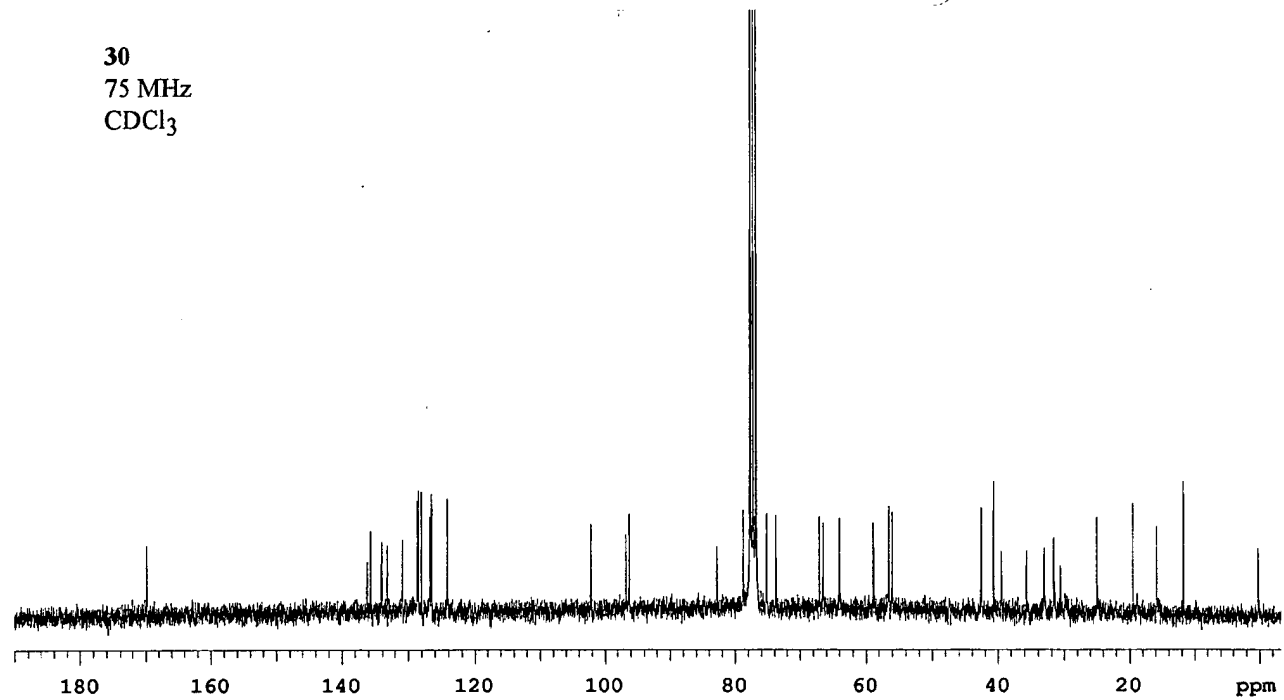


FIG. 43

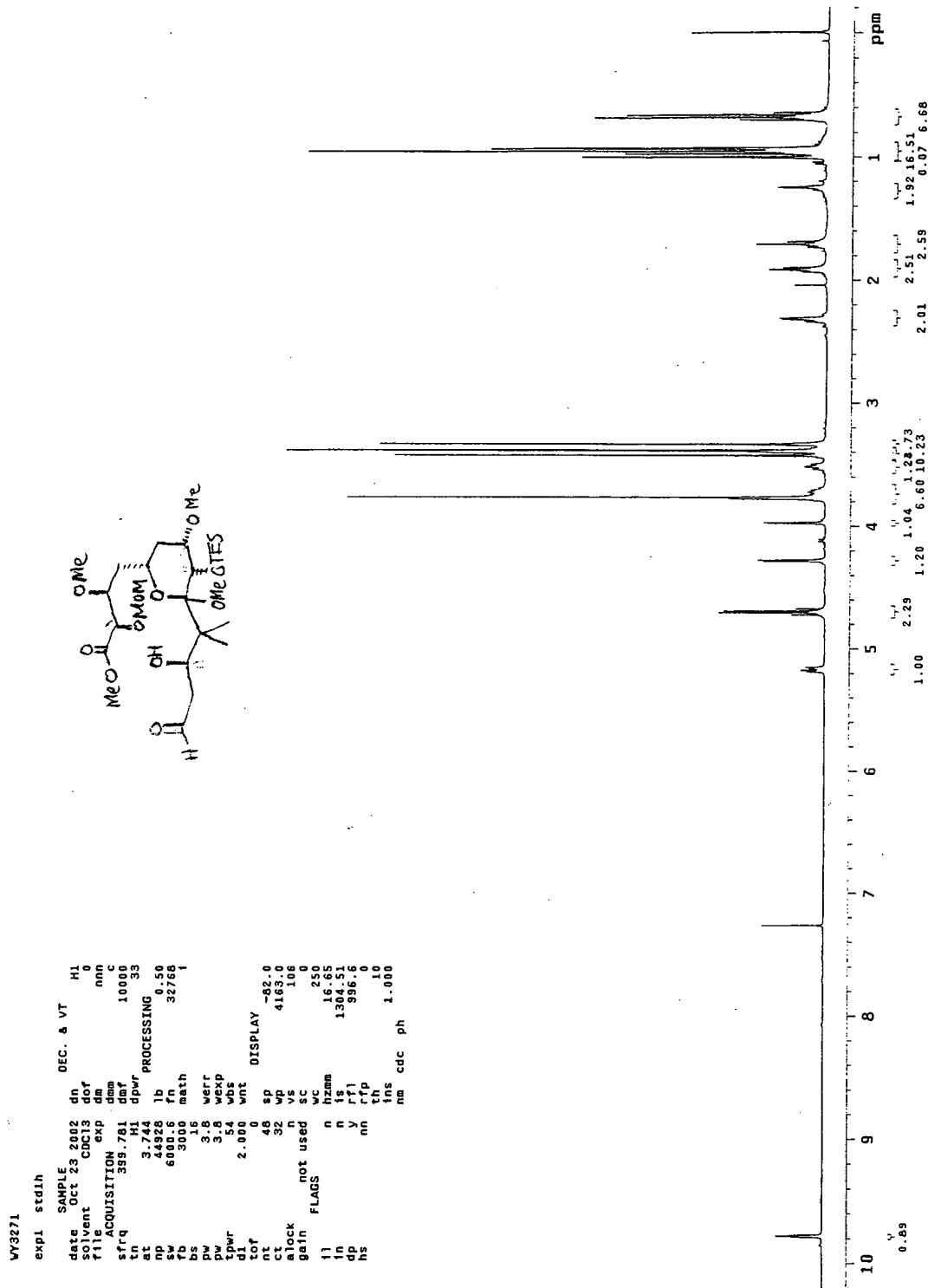
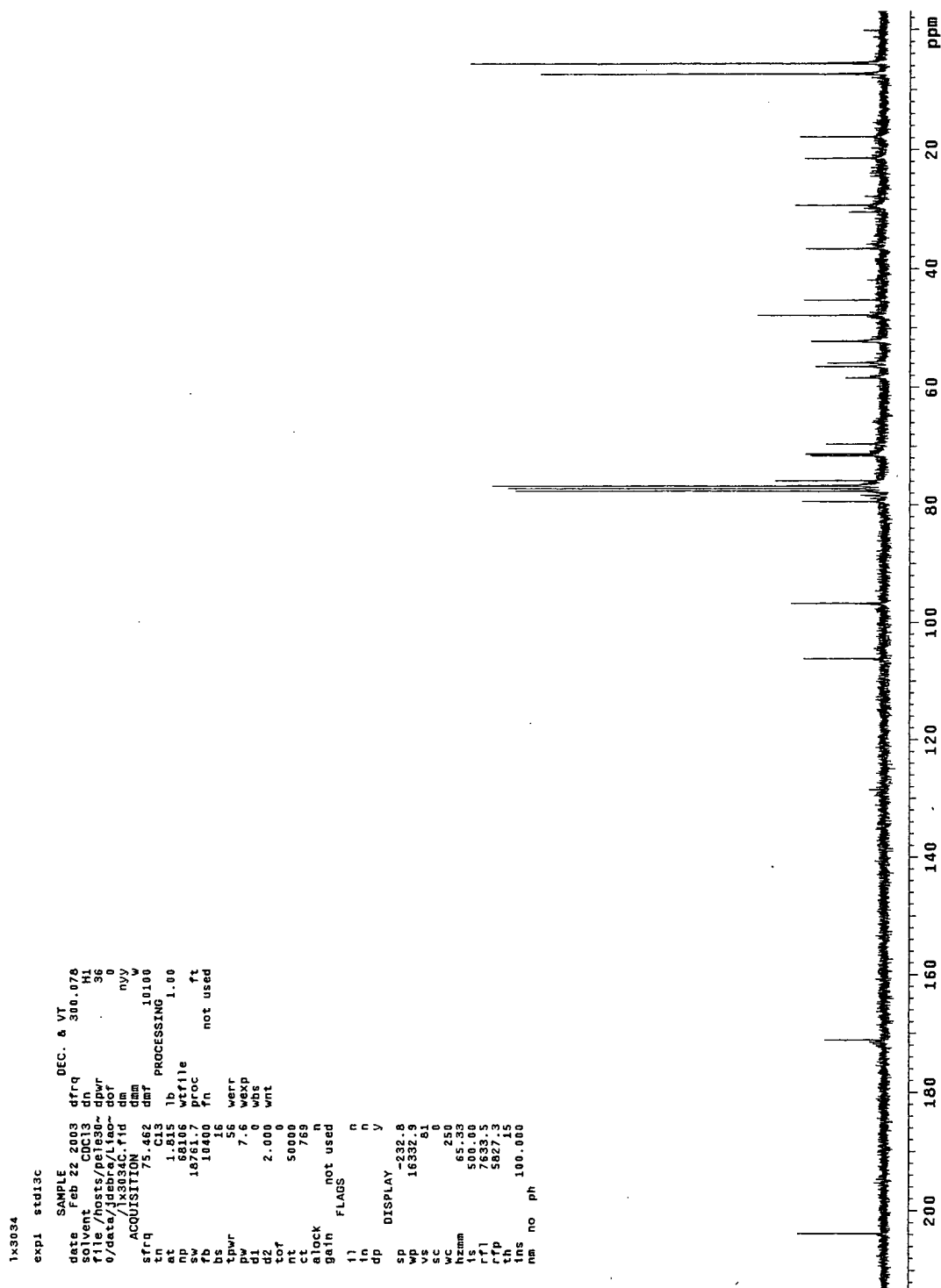
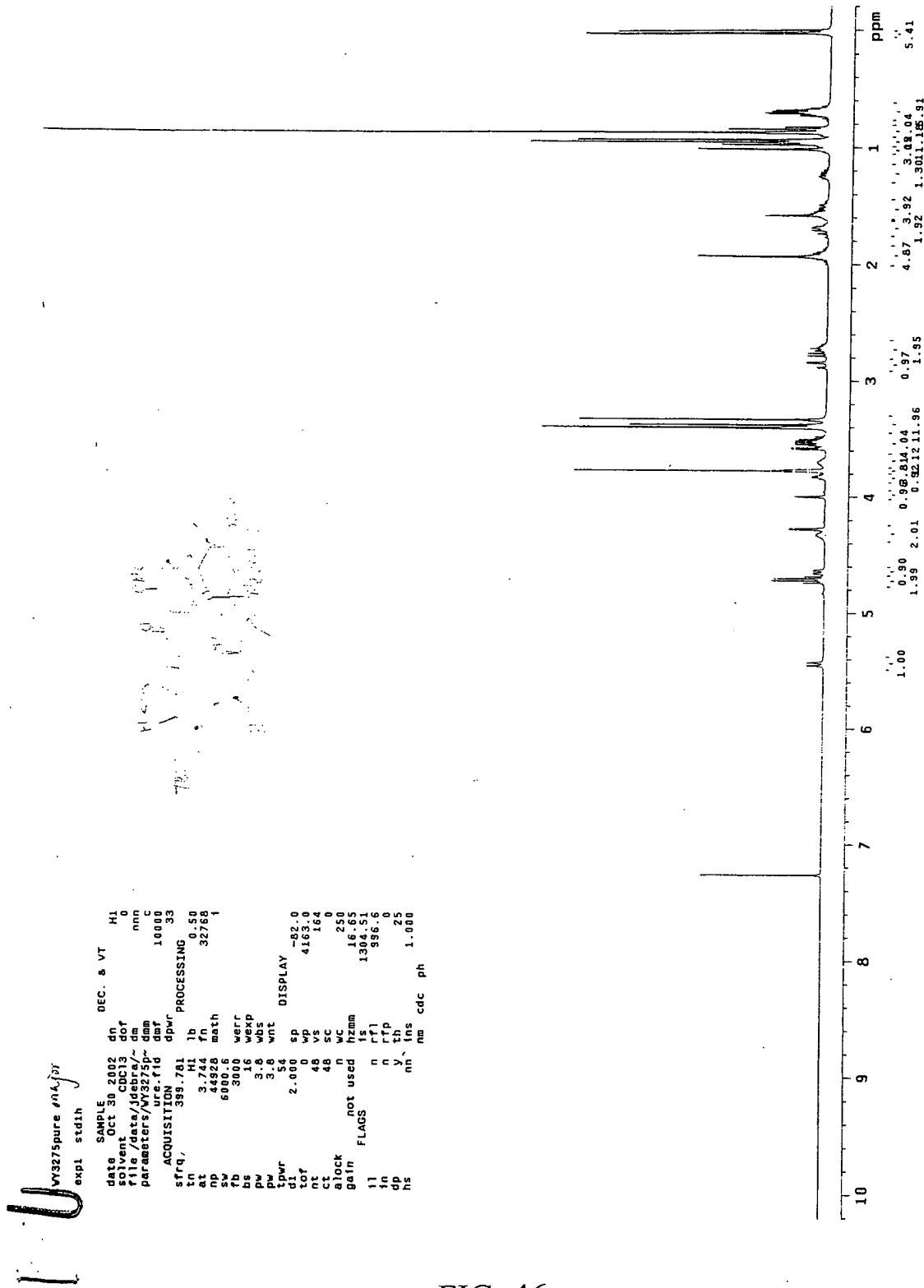


FIG. 44





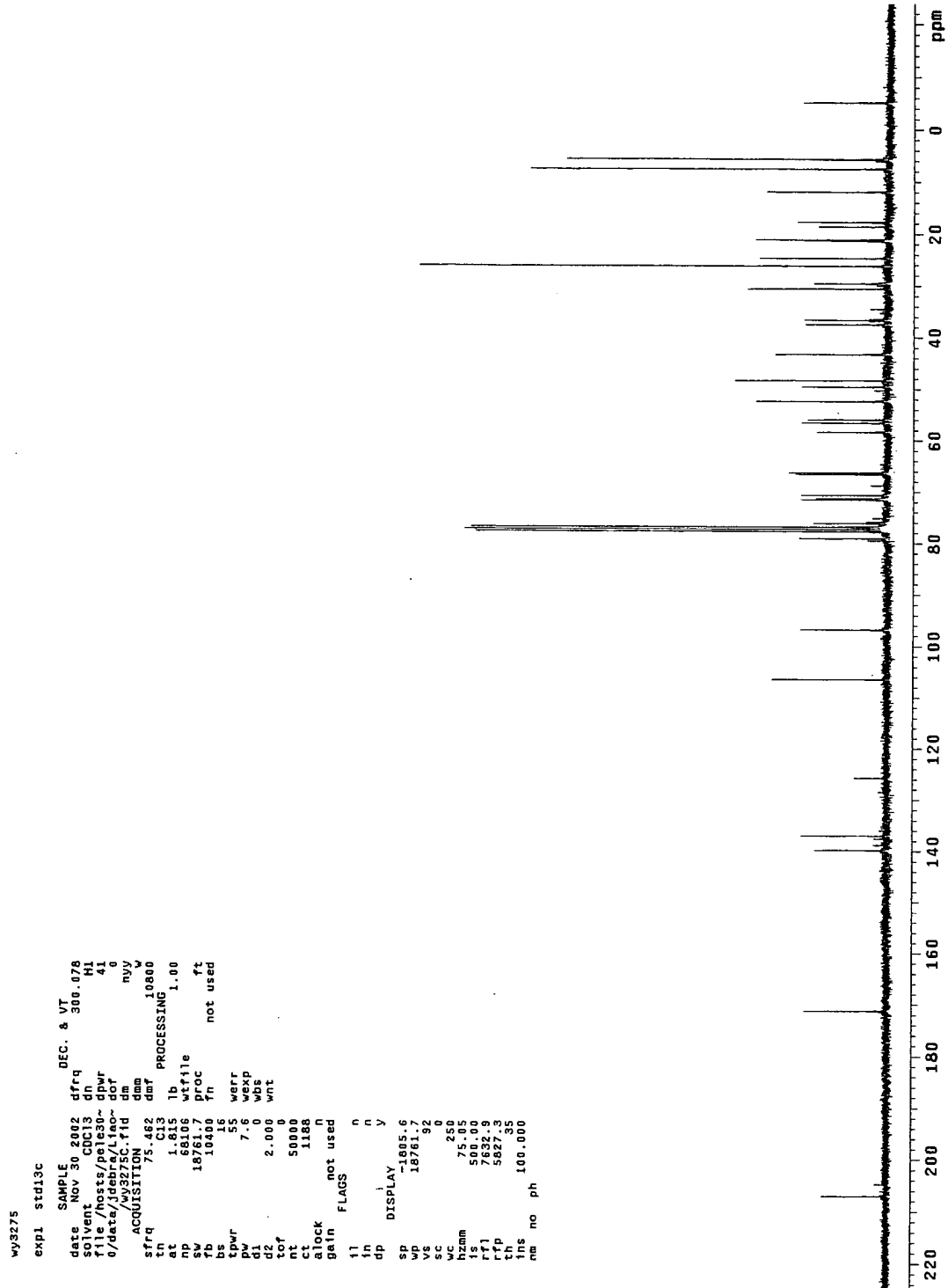


FIG. 47

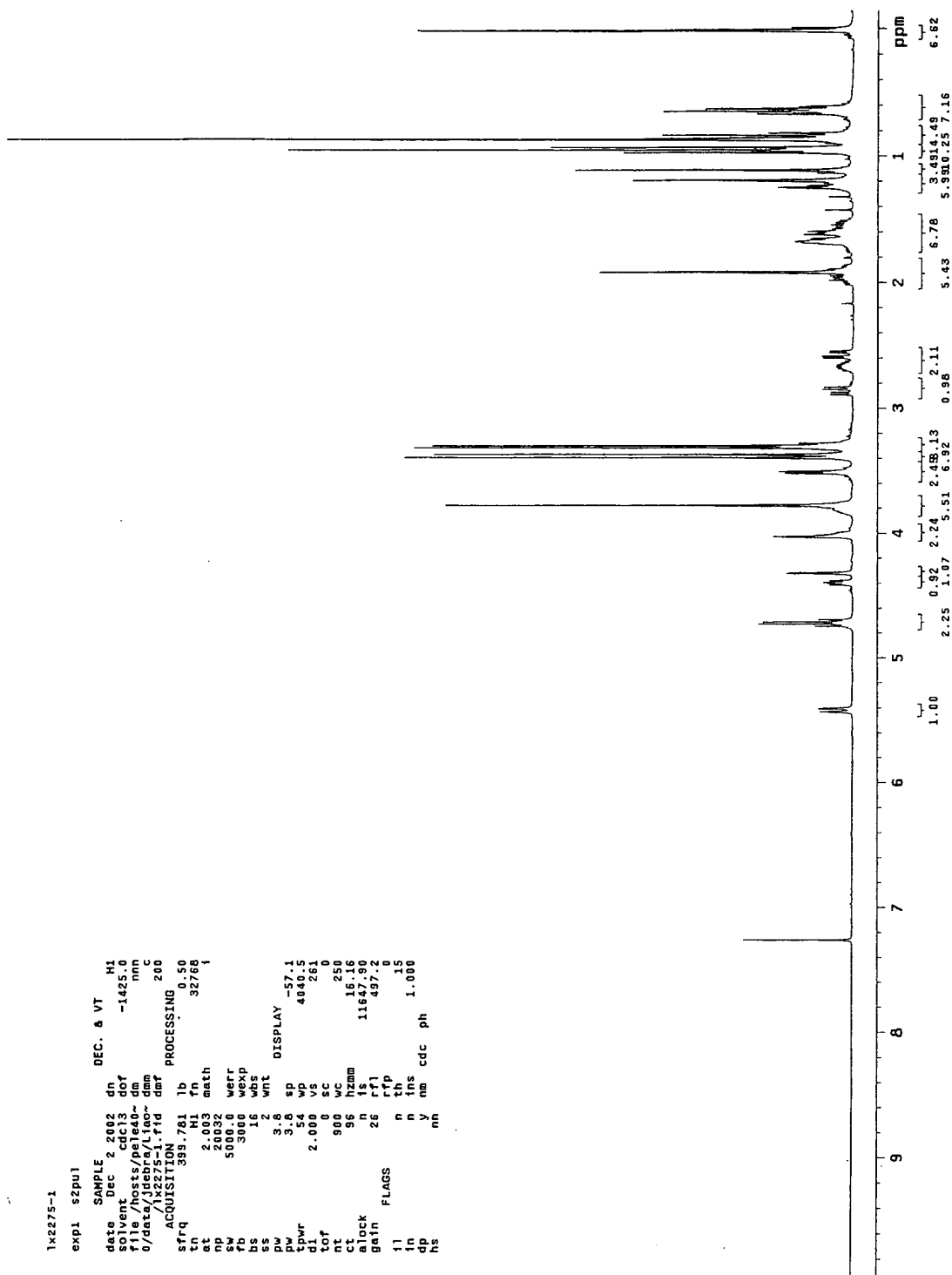
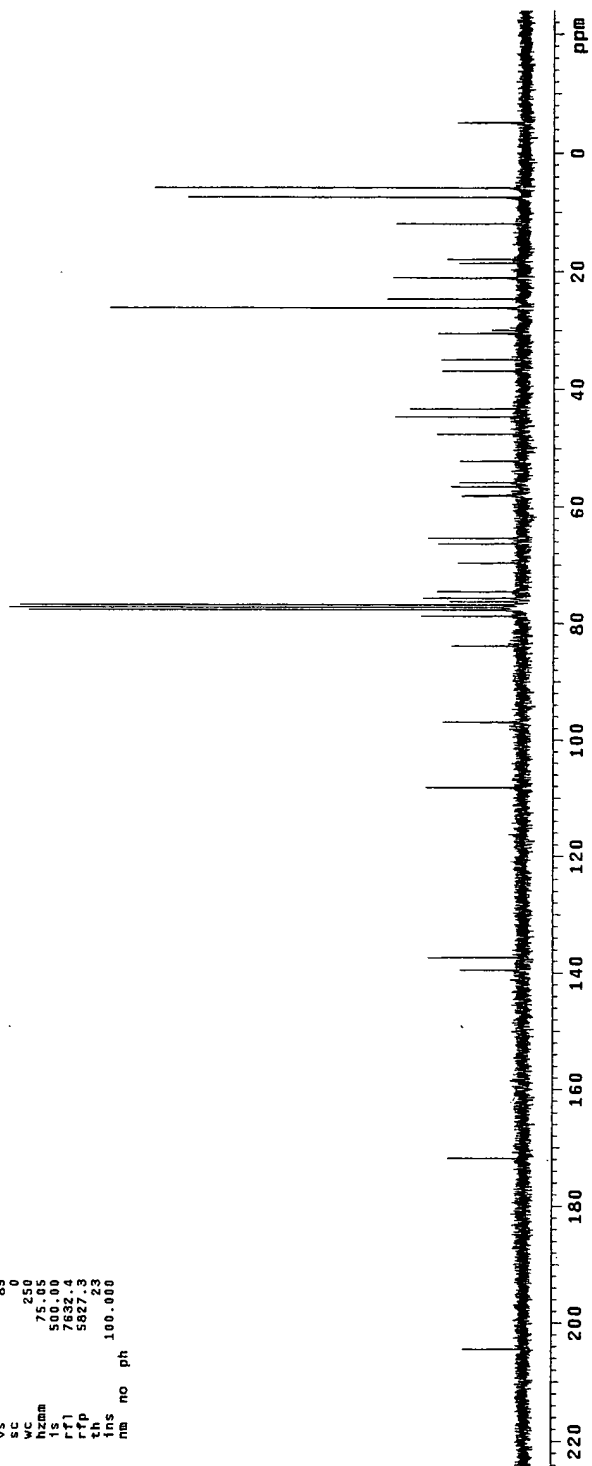


FIG. 48

- }
i

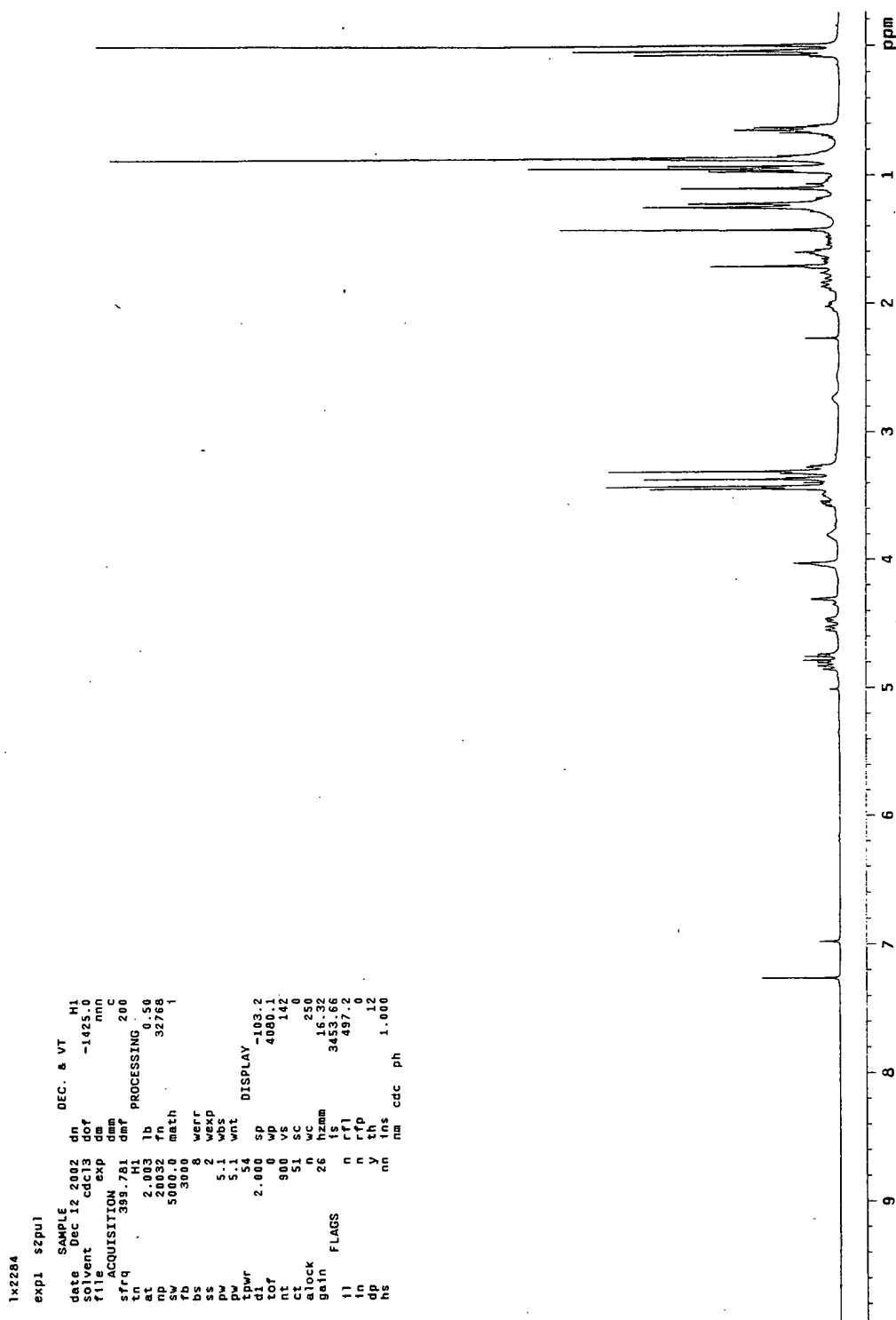


FIG. 50

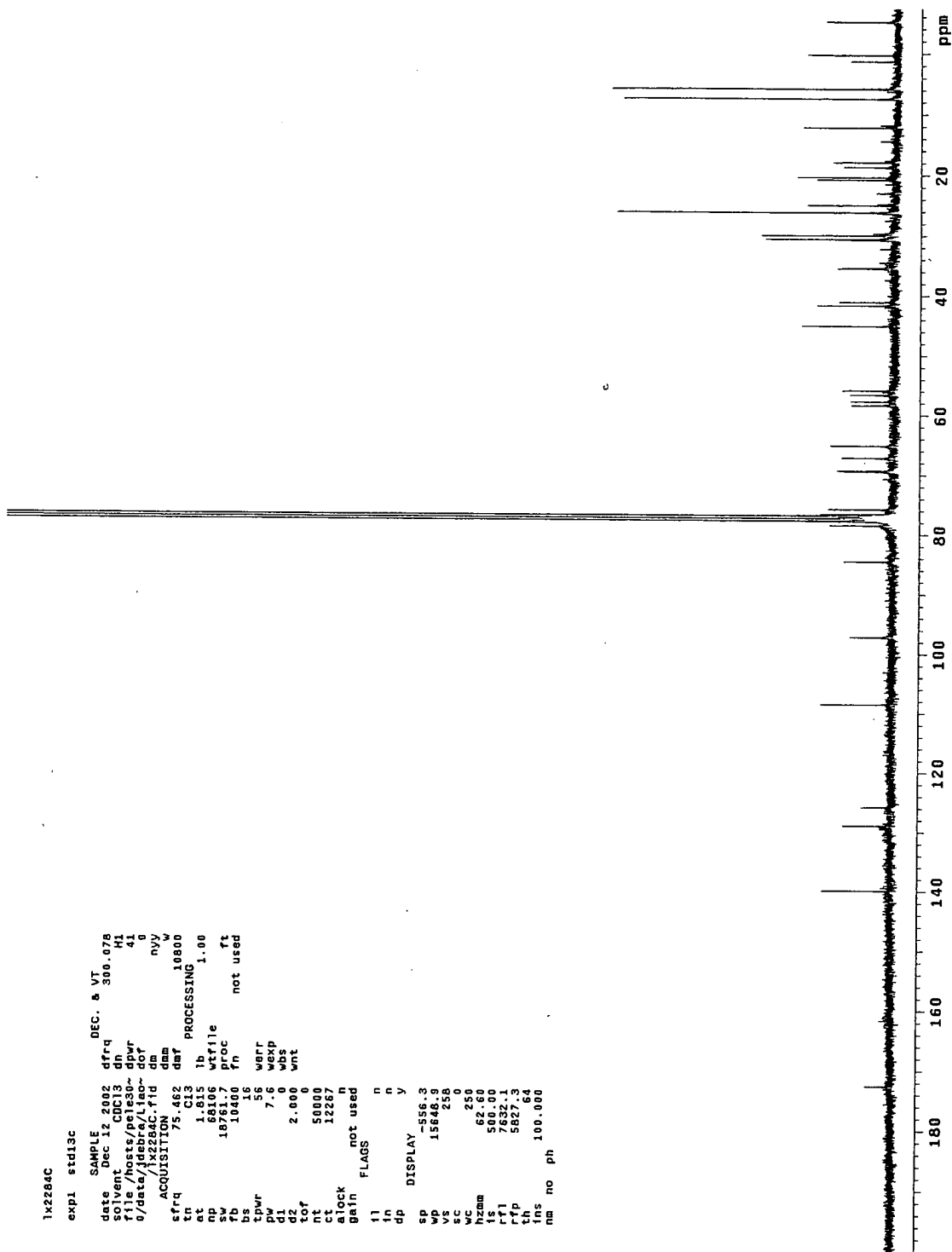


FIG. 51

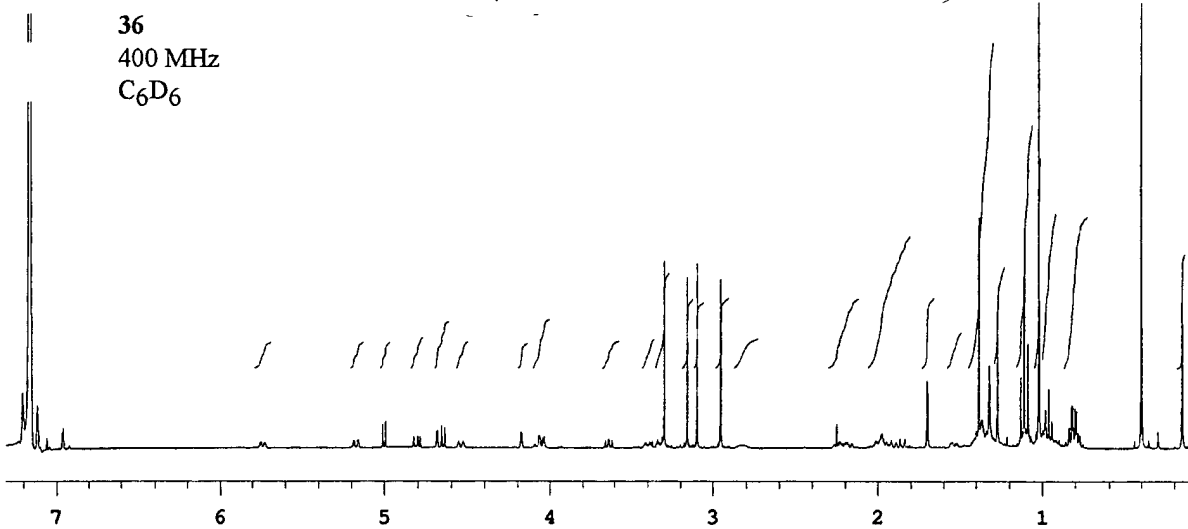


FIG. 52

36 1D-NOE Irradiation at 5.74 ppm

400 MHz

C₆D₆

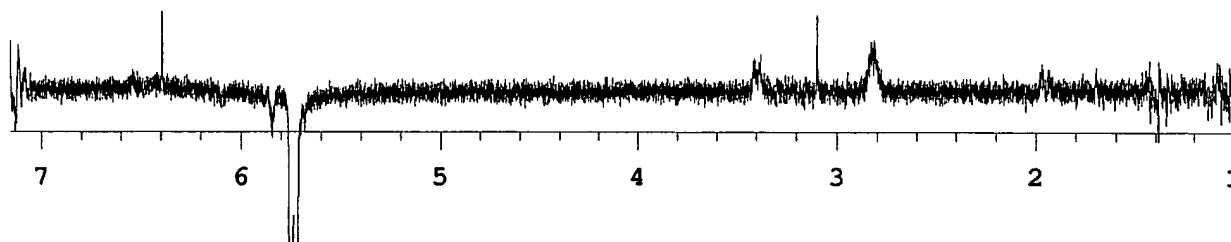


FIG. 53

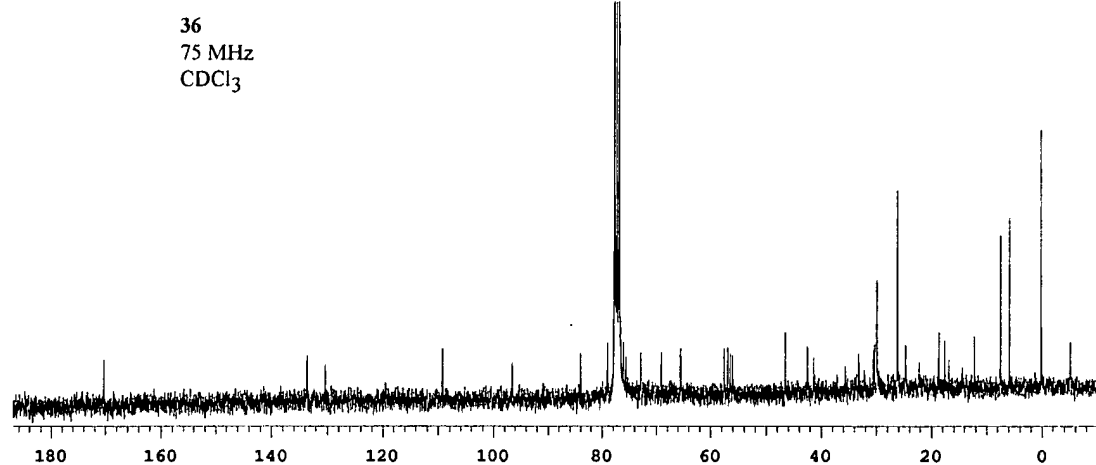


FIG. 54

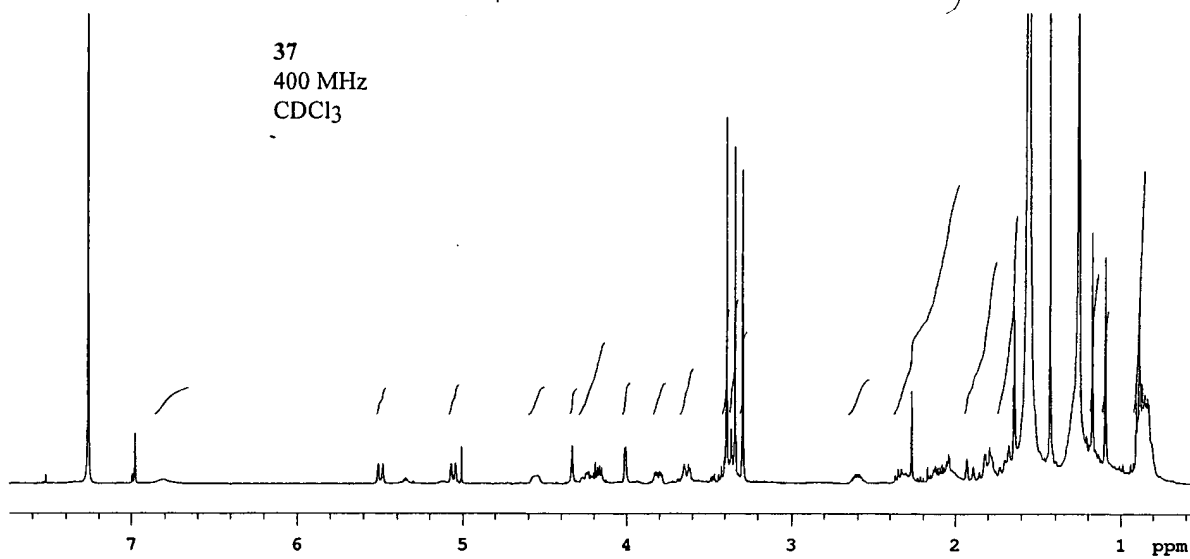


FIG. 55

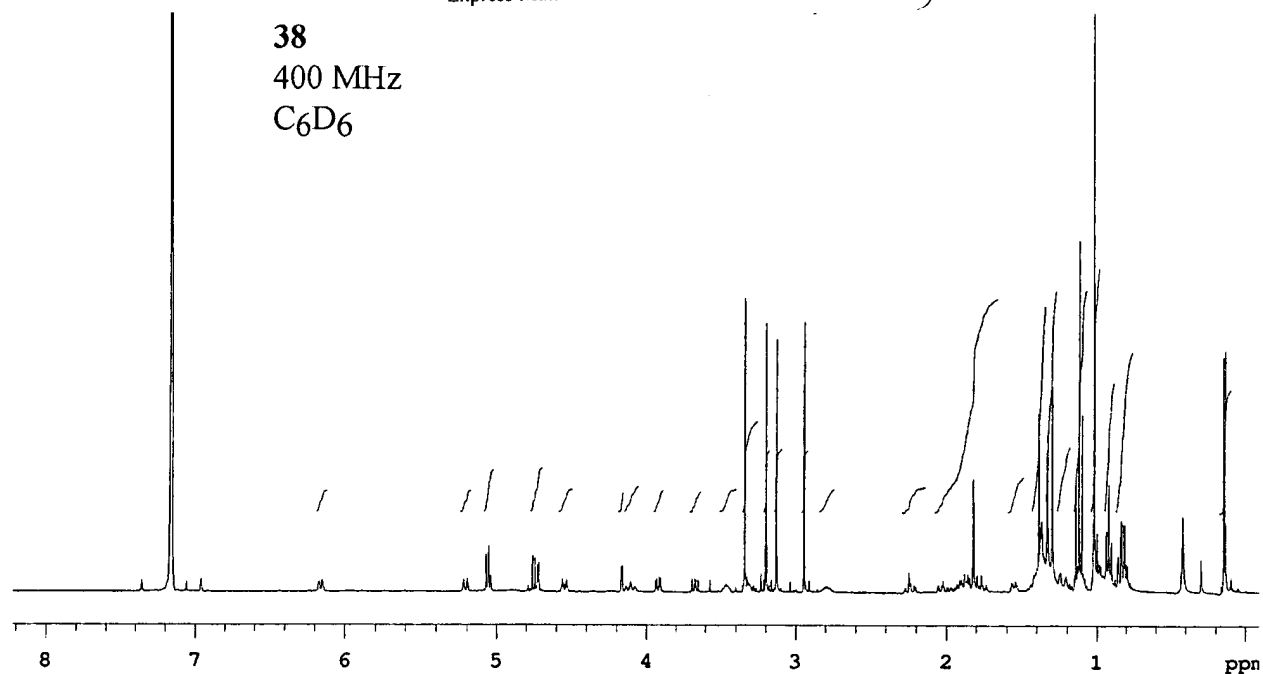


FIG. 56

38
400 MHz
CDCl₃

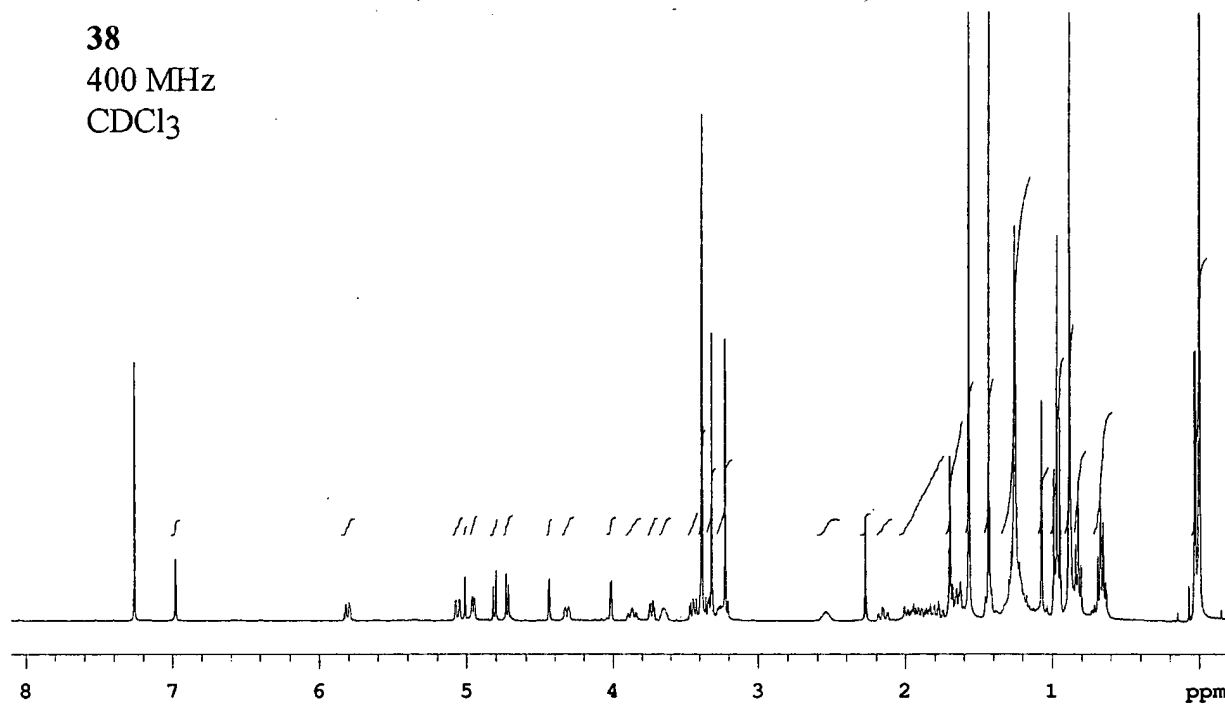


FIG. 57

38 1D-NOE Irradiation at 6.16 ppm
400 MHz
C₆D₆

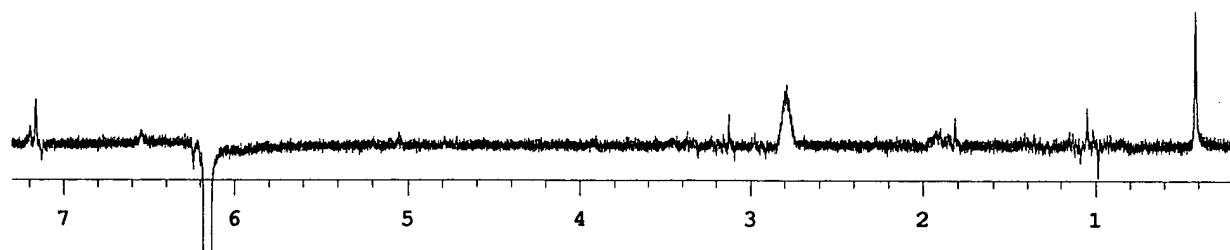


FIG. 58

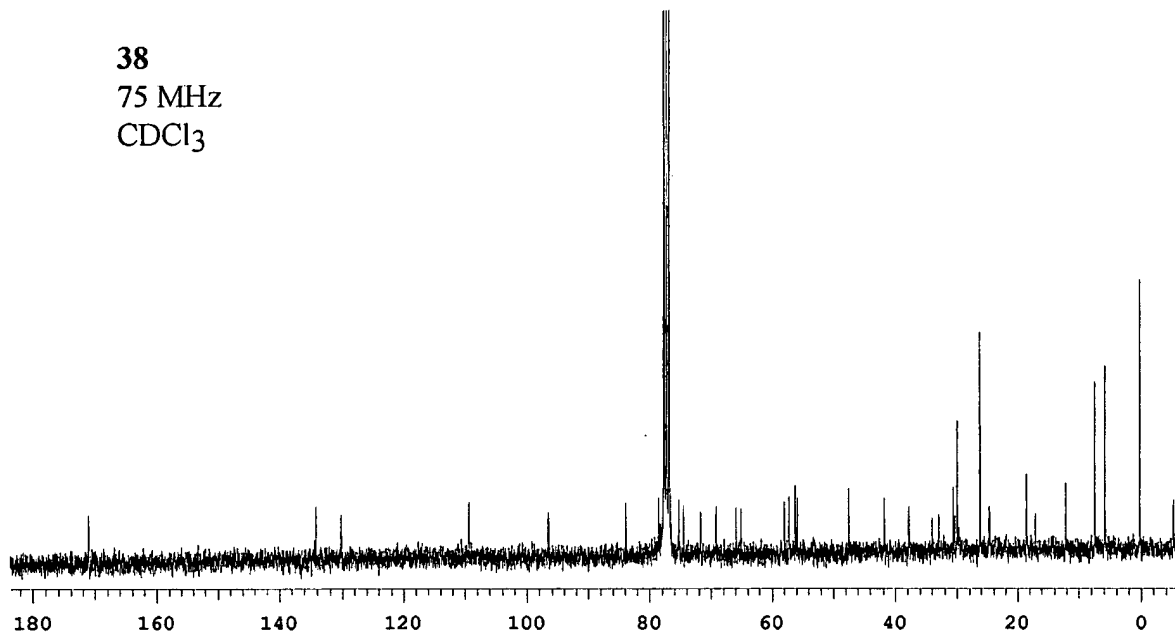


FIG. 59

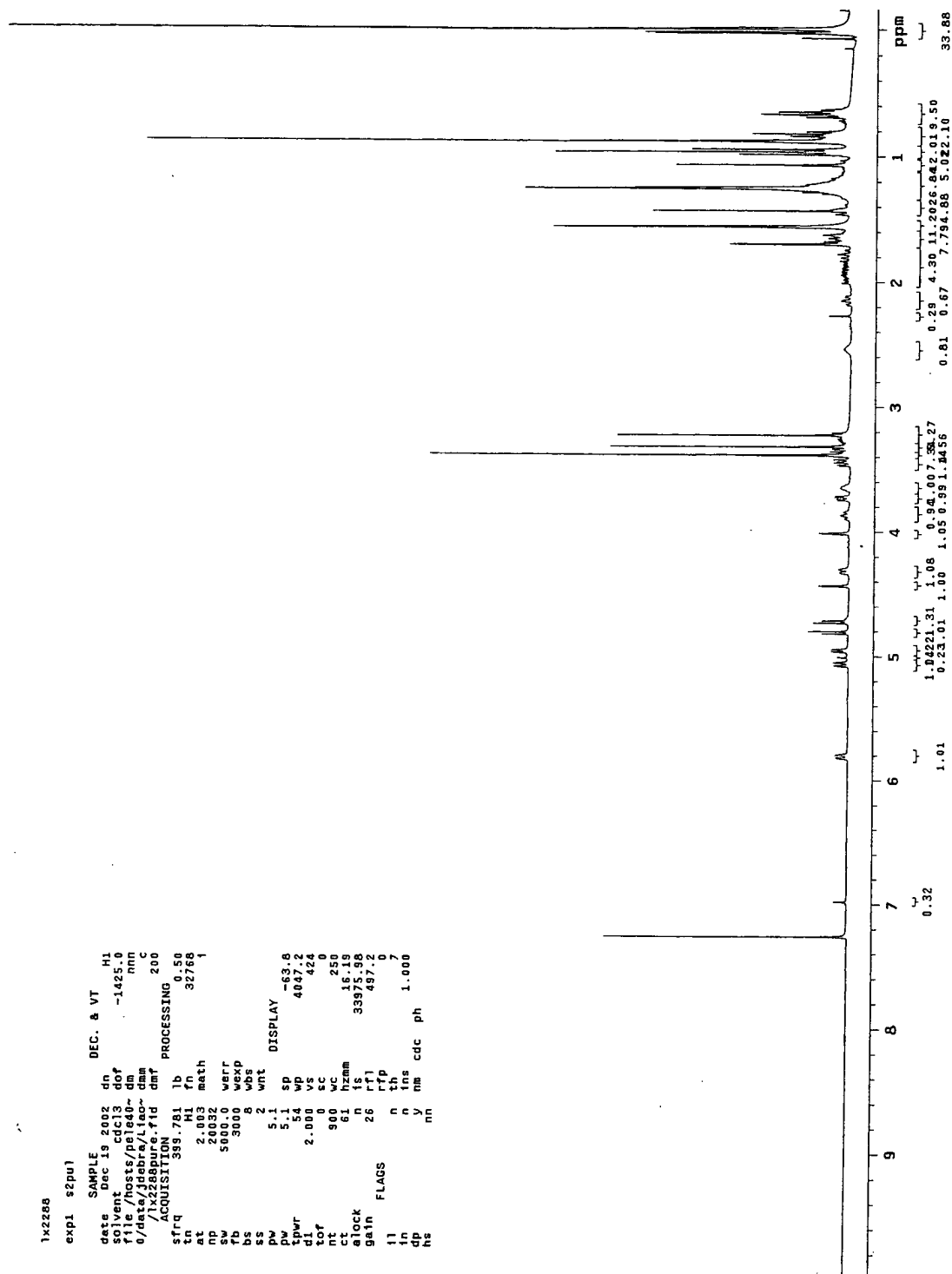


FIG. 60

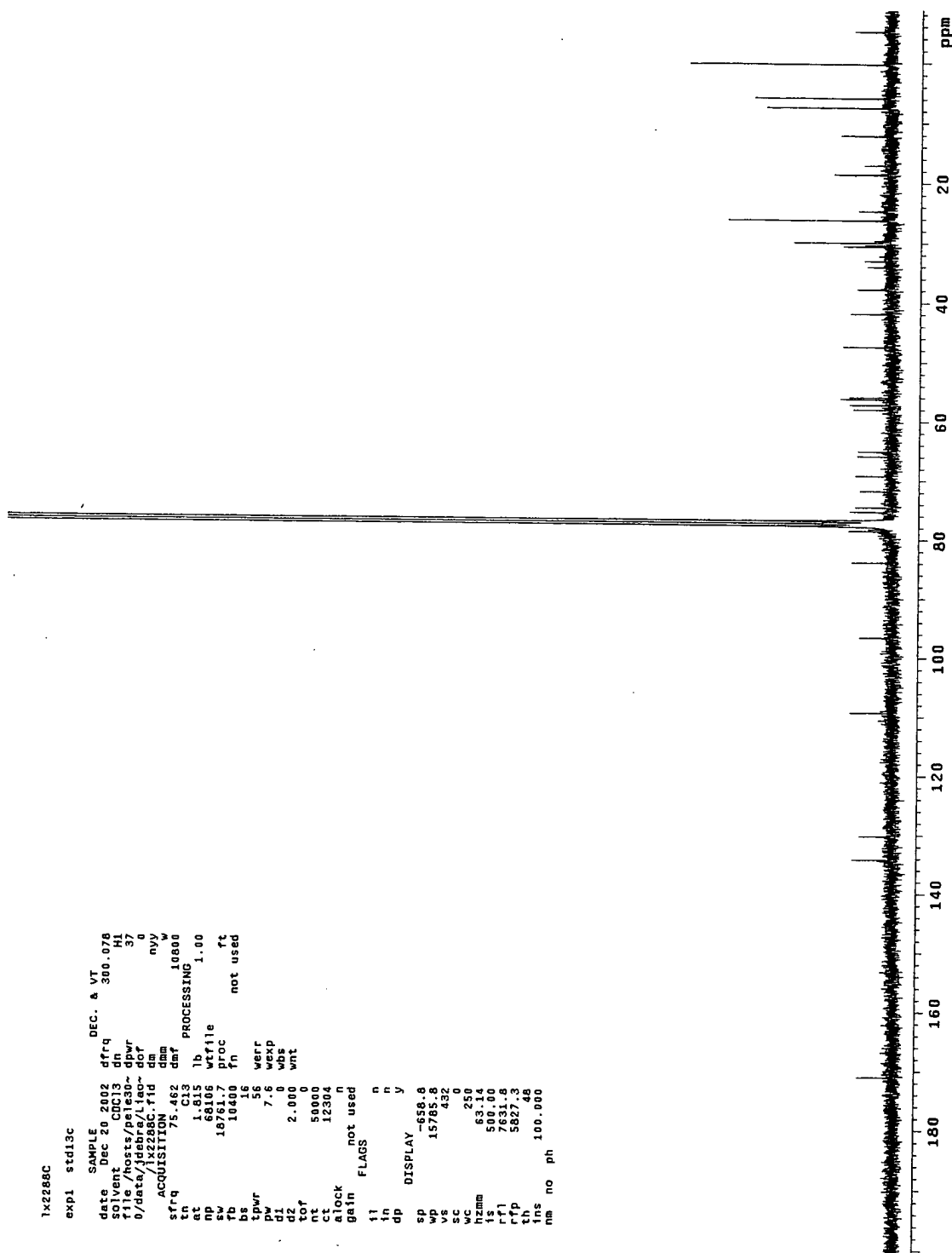


FIG. 61

FIG. 62

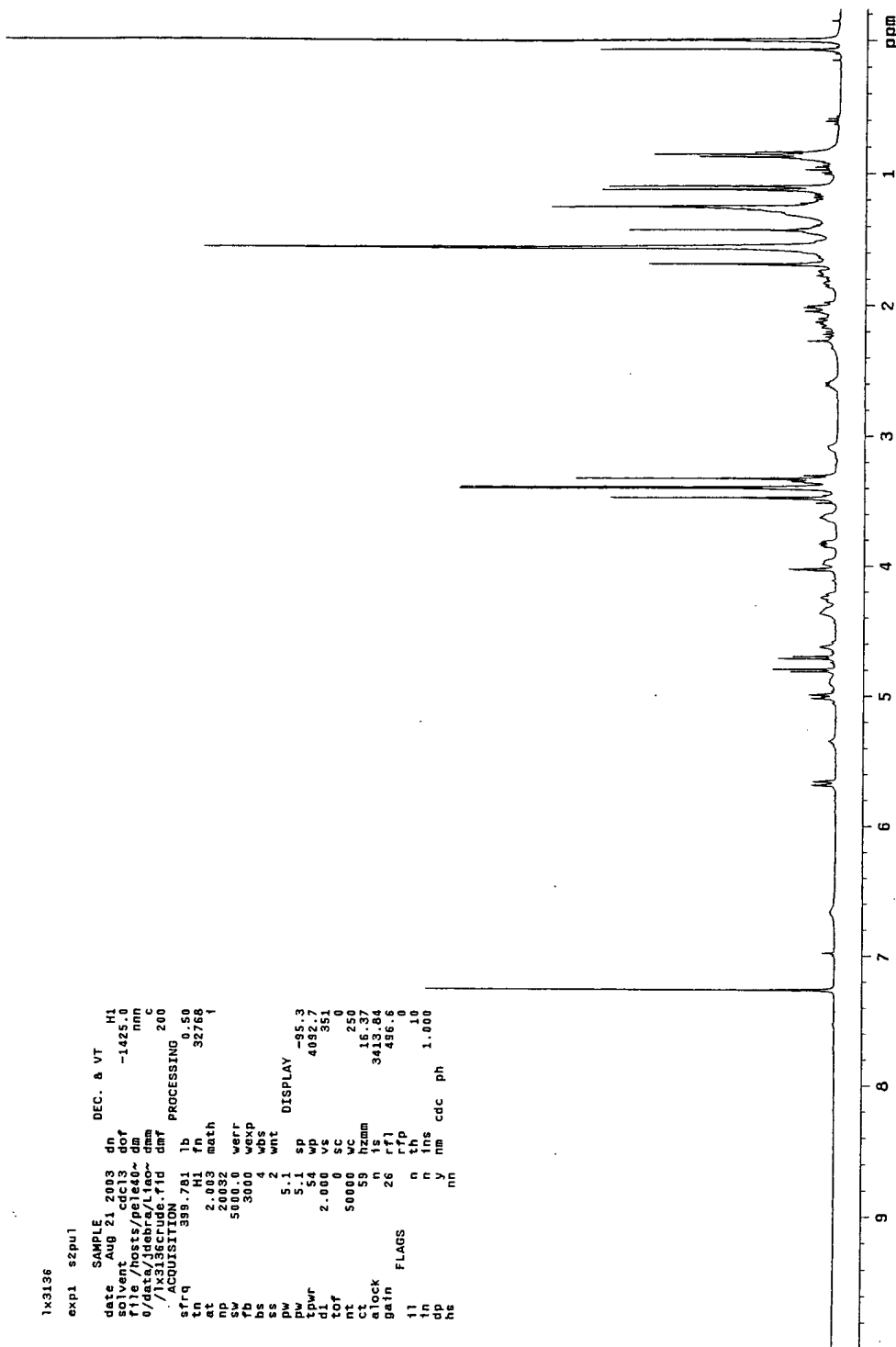


FIG. 63

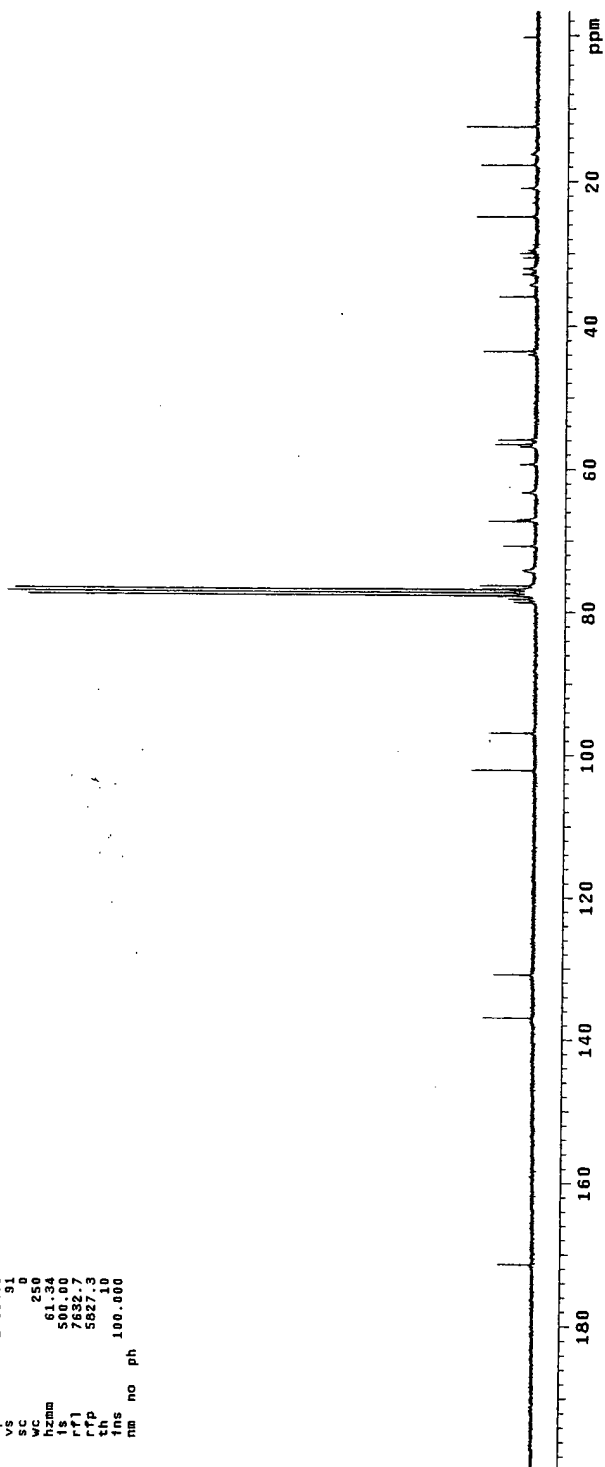


FIG. 64

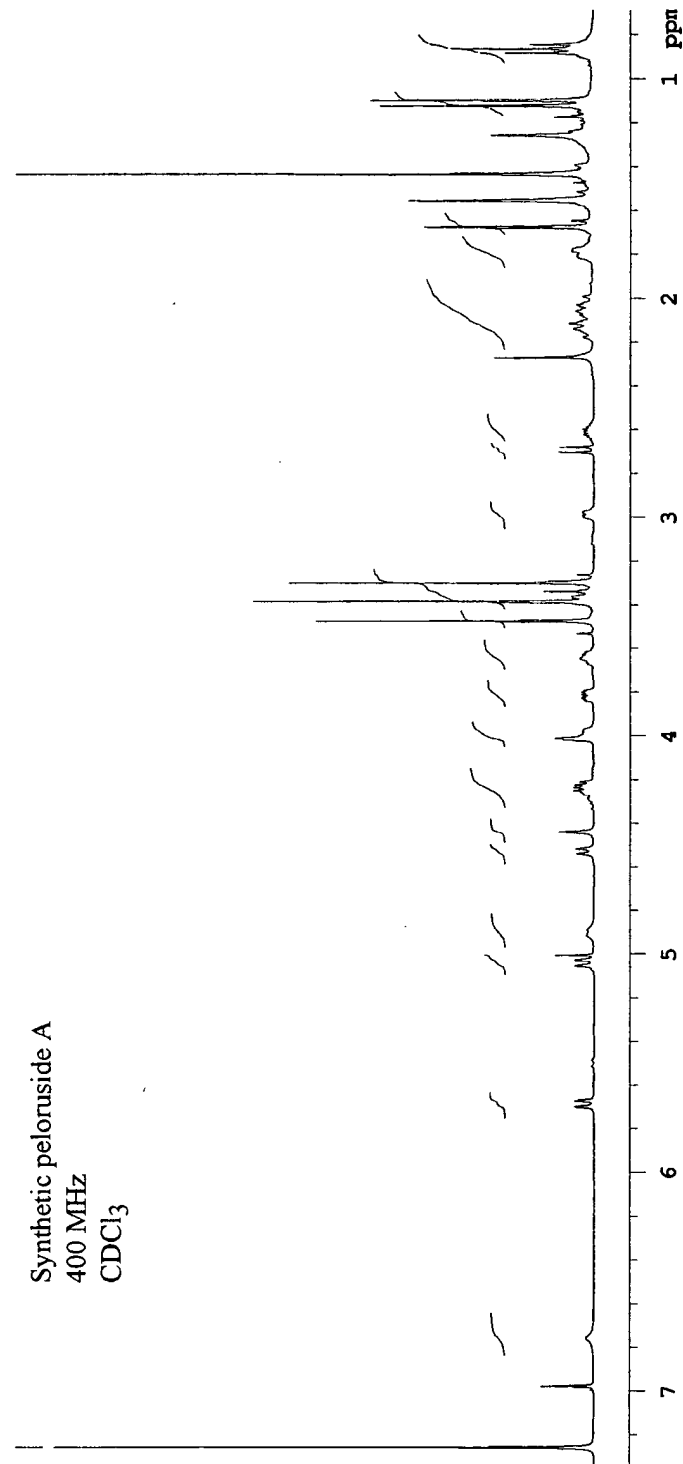


FIG. 65

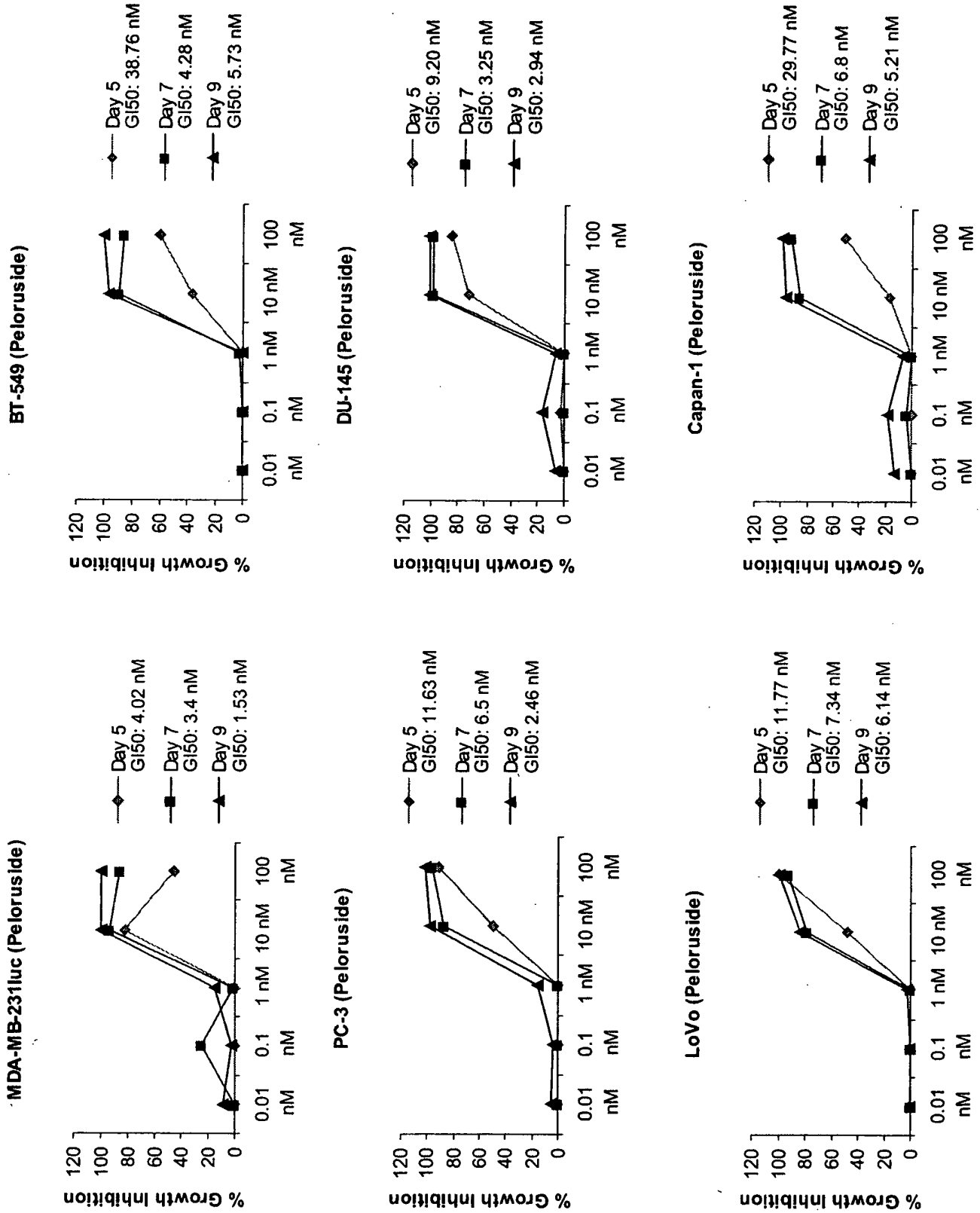


FIG. 66

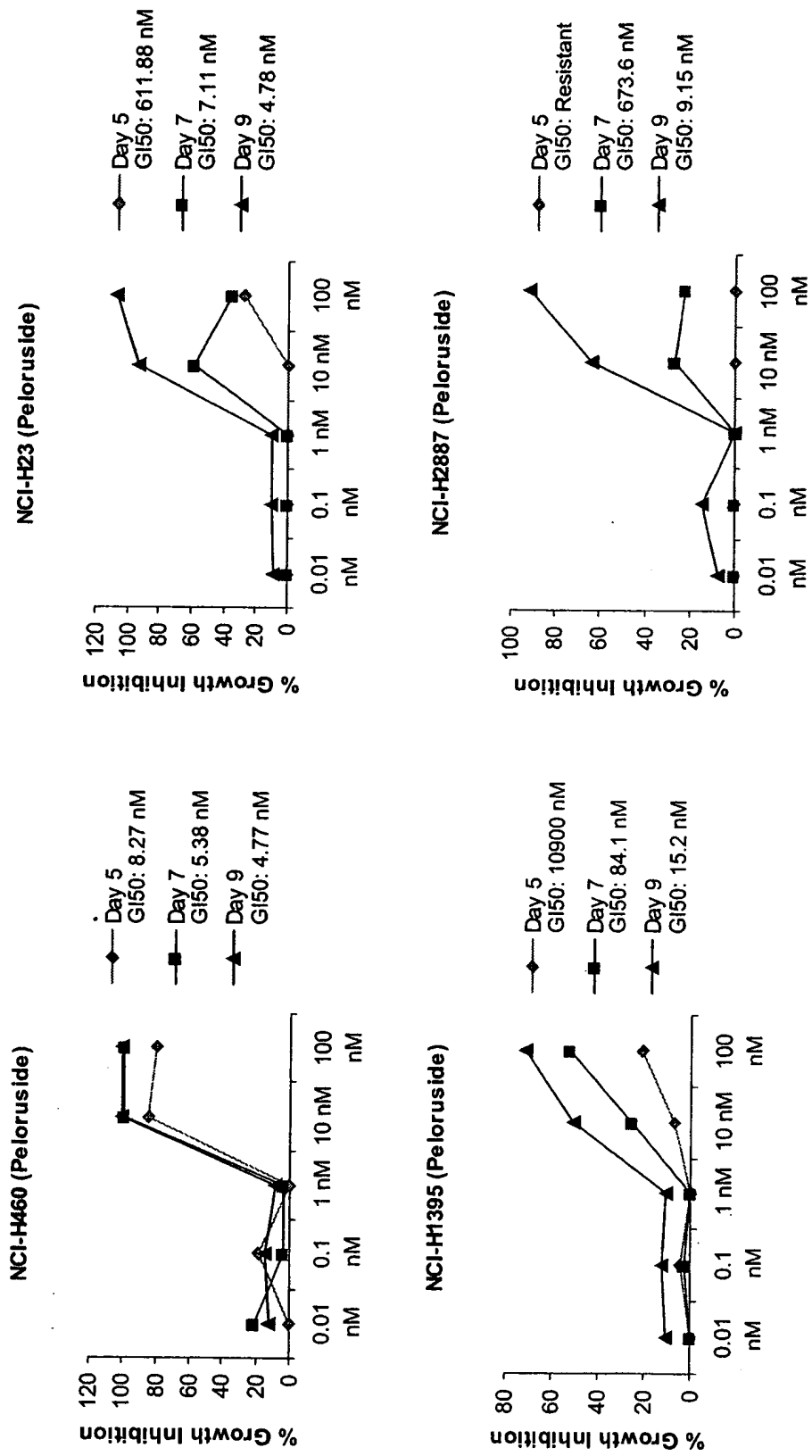
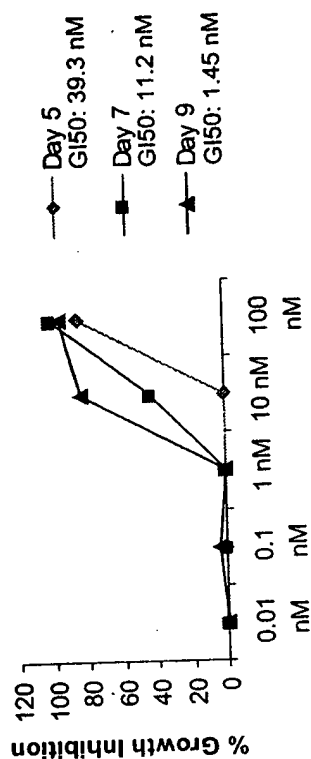
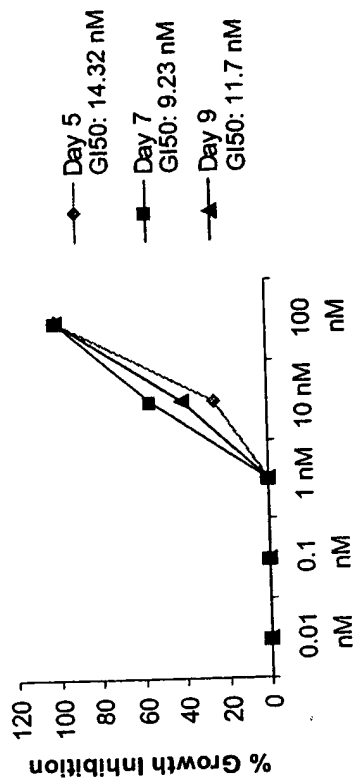


FIG. 67

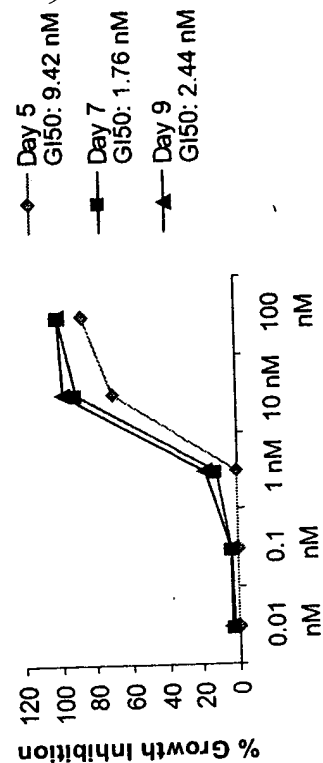
SK-HEP-1 (Peloruside)



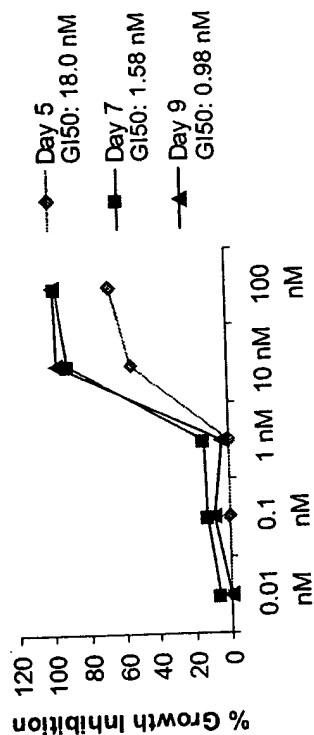
HCT-15 (Peloruside)



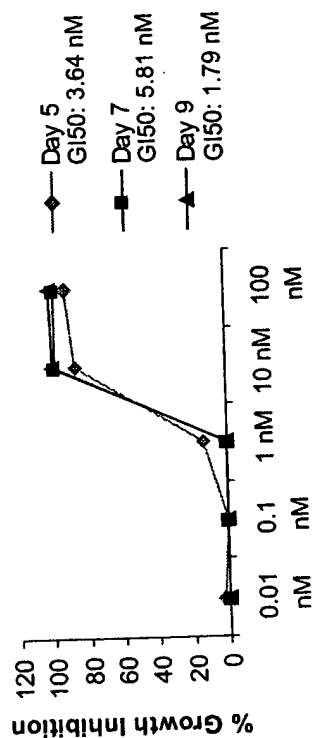
SK-MEL-5 (Peloruside)



Hep-G2 (Peloruside)



HCT-116 (Peloruside)



SK-MEL-28 (Peloruside)

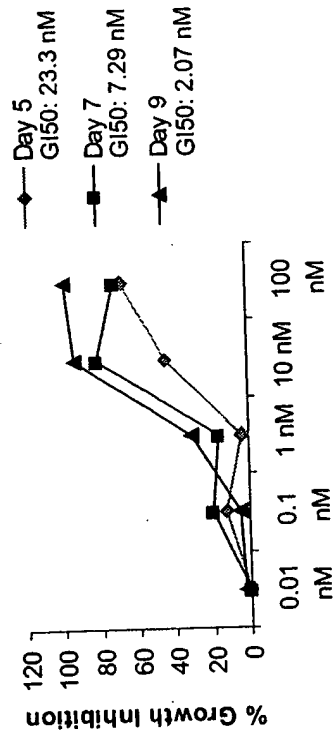


FIG. 68

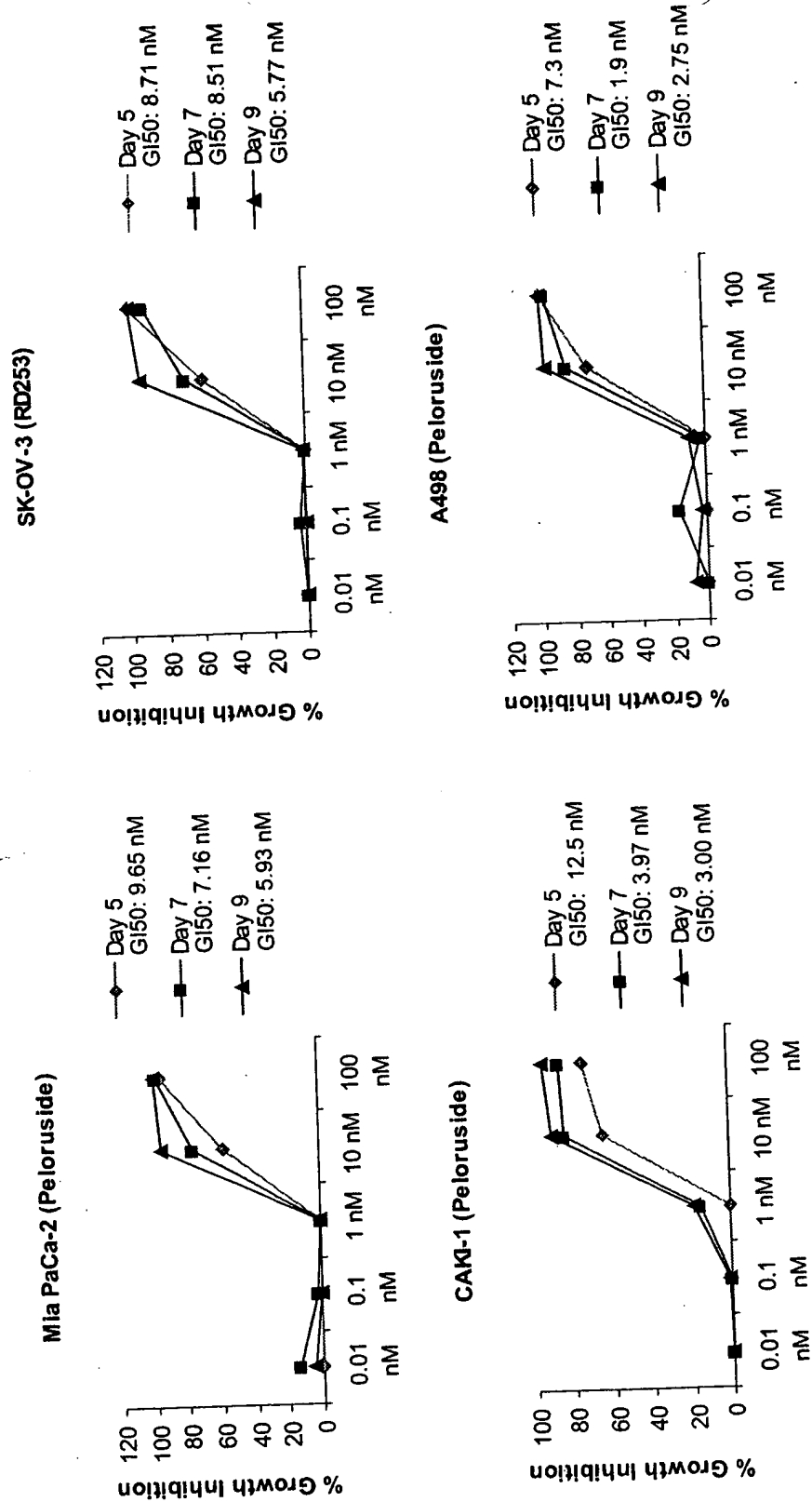


FIG. 69

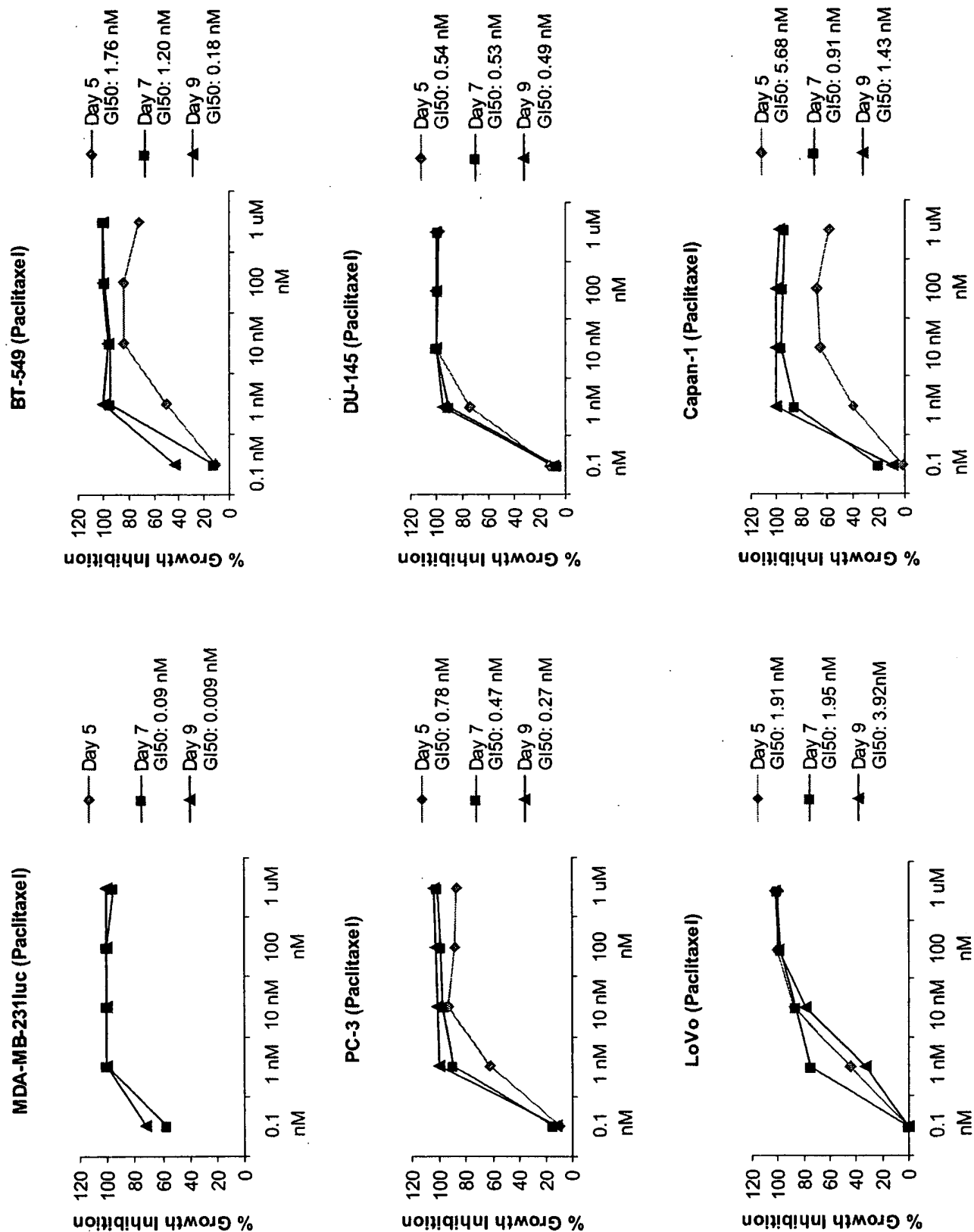


FIG. 70

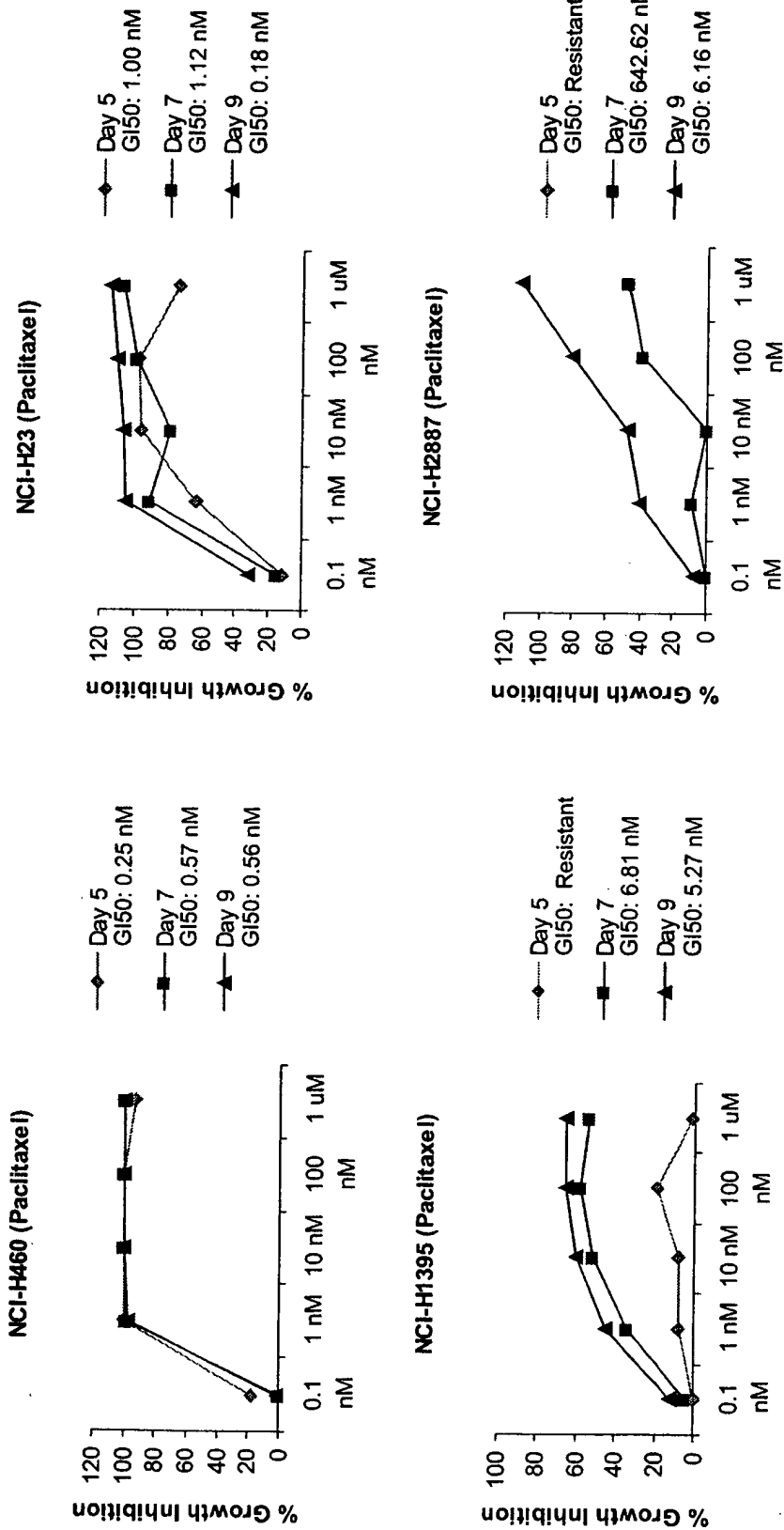


FIG. 71

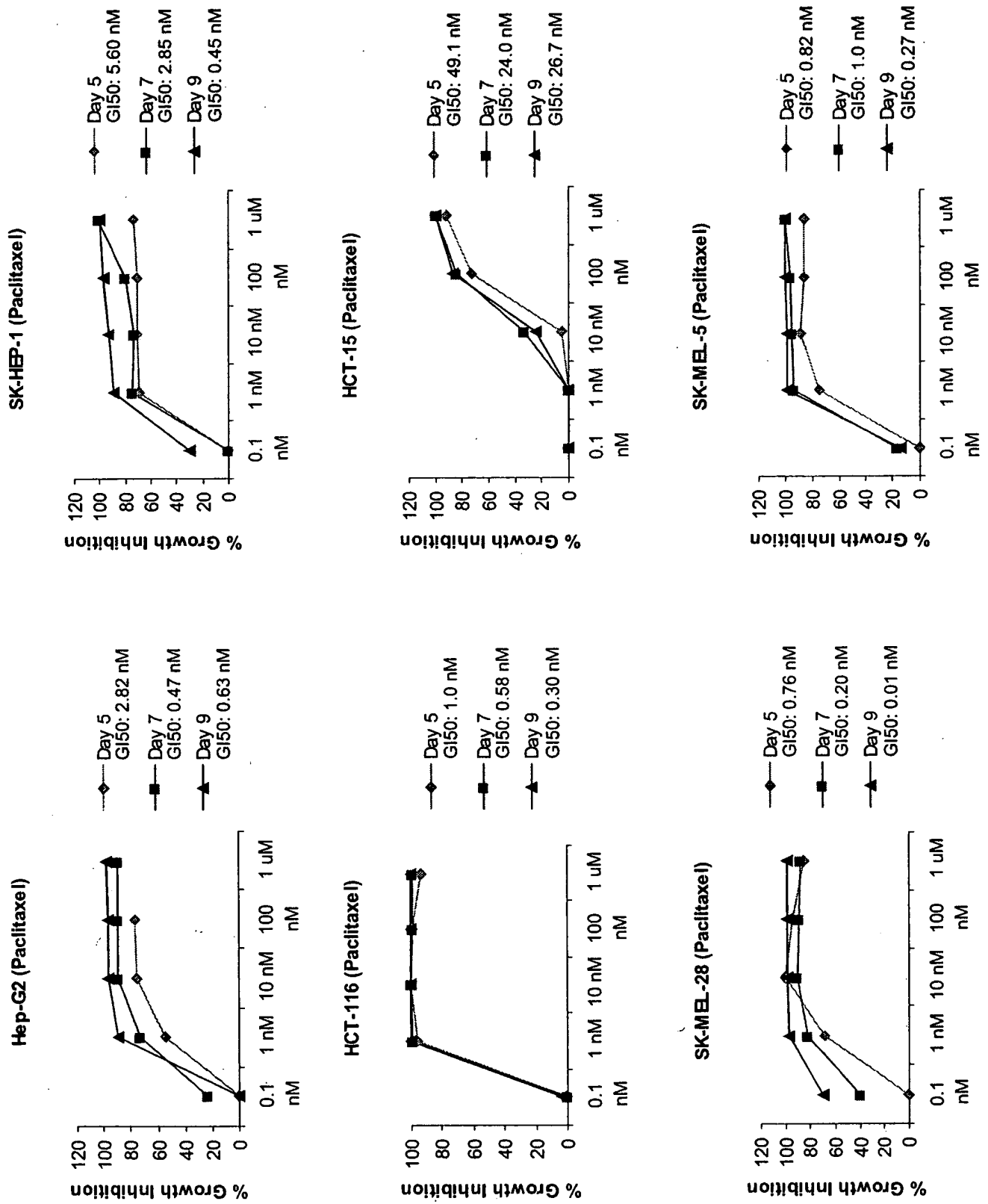


FIG. 72

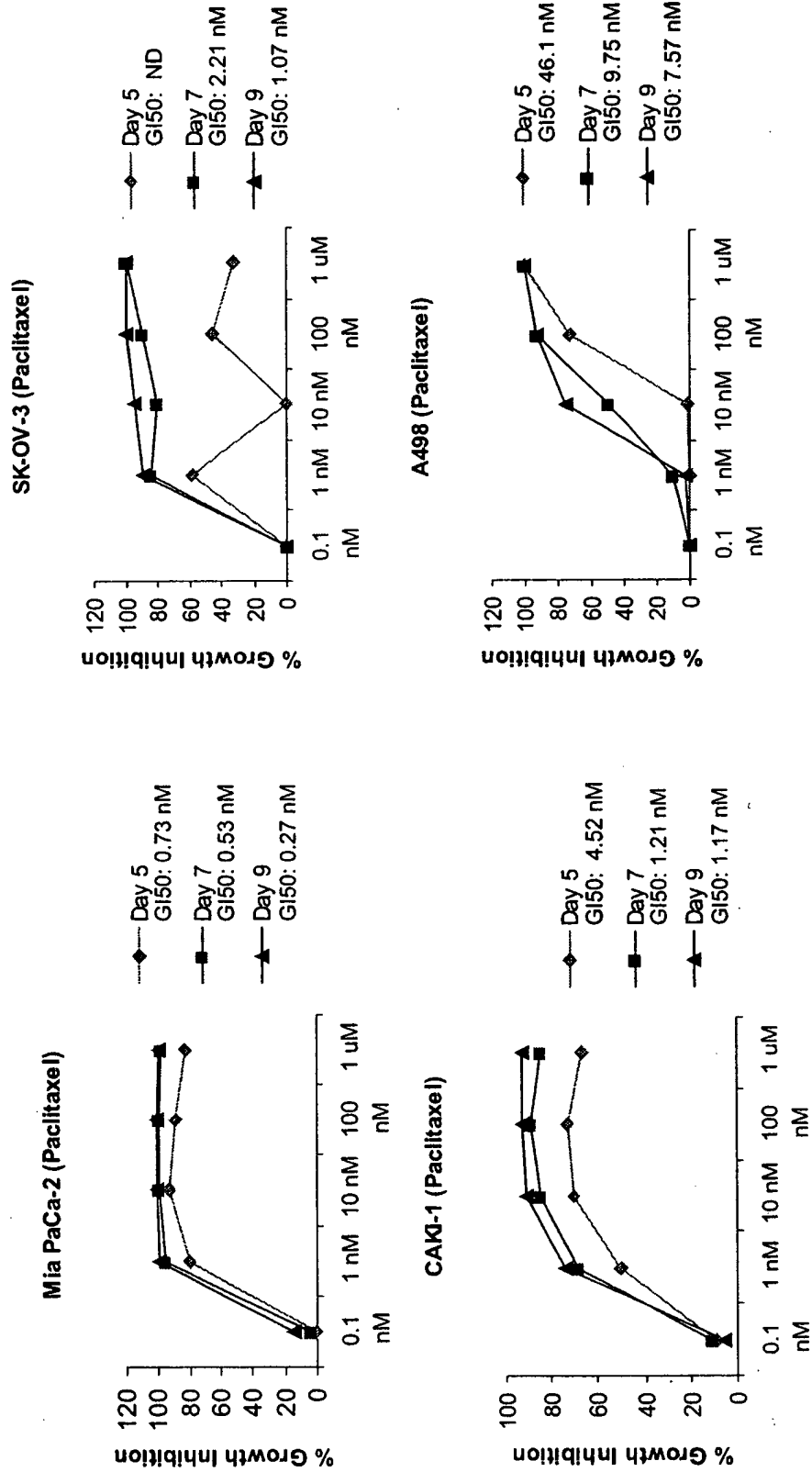


FIG. 73

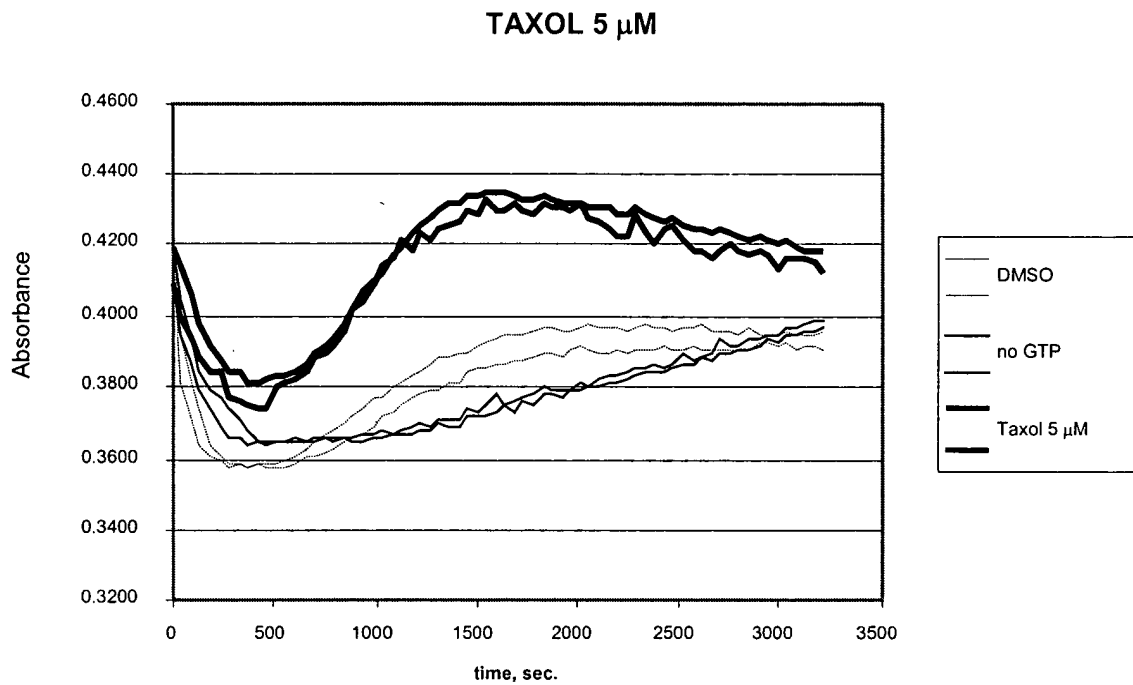
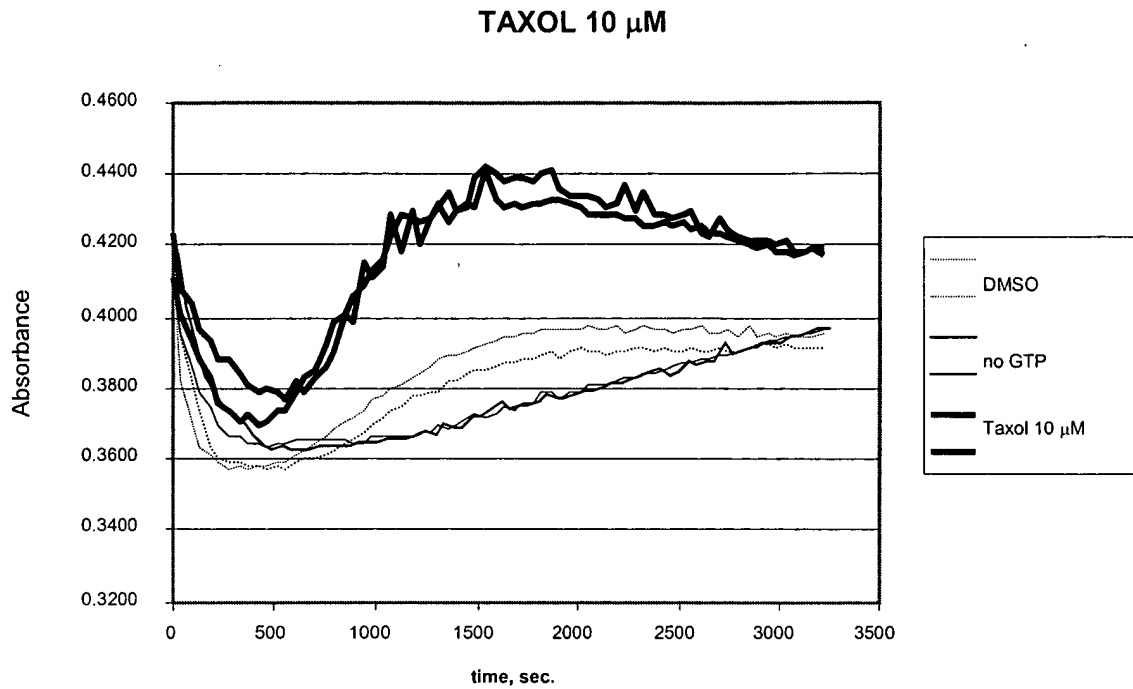
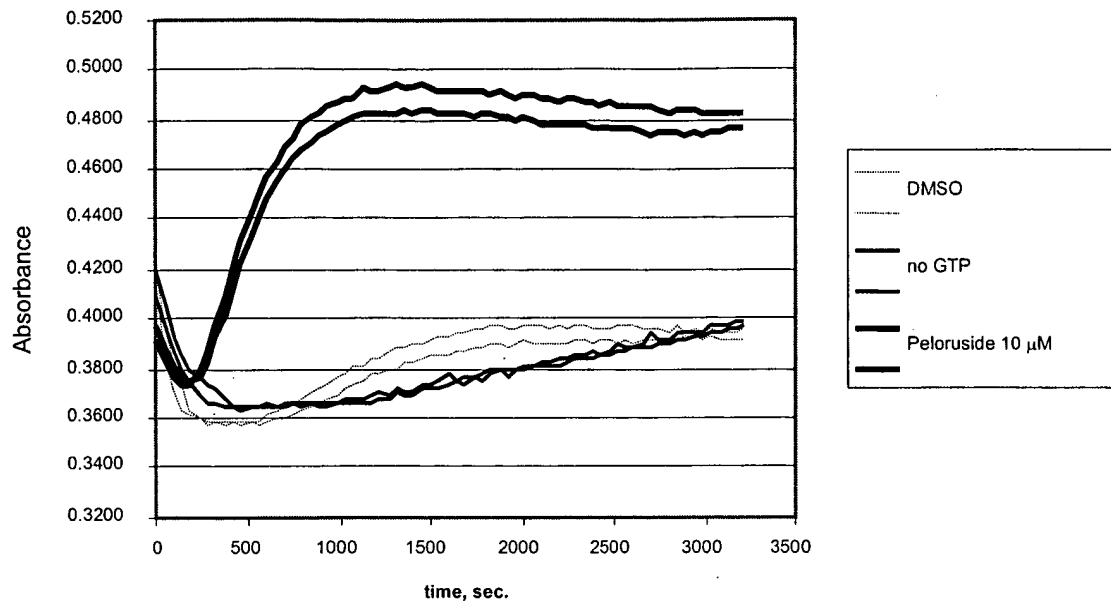


FIG. 74

PELORUSIDE 10 μ M



PELORUSIDE 5 μ M

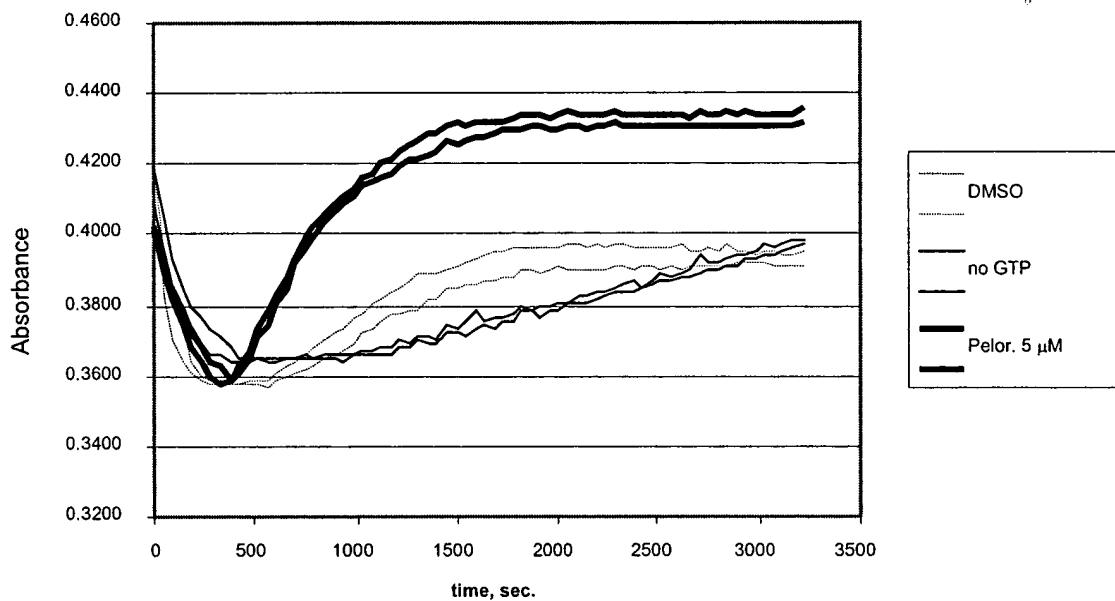
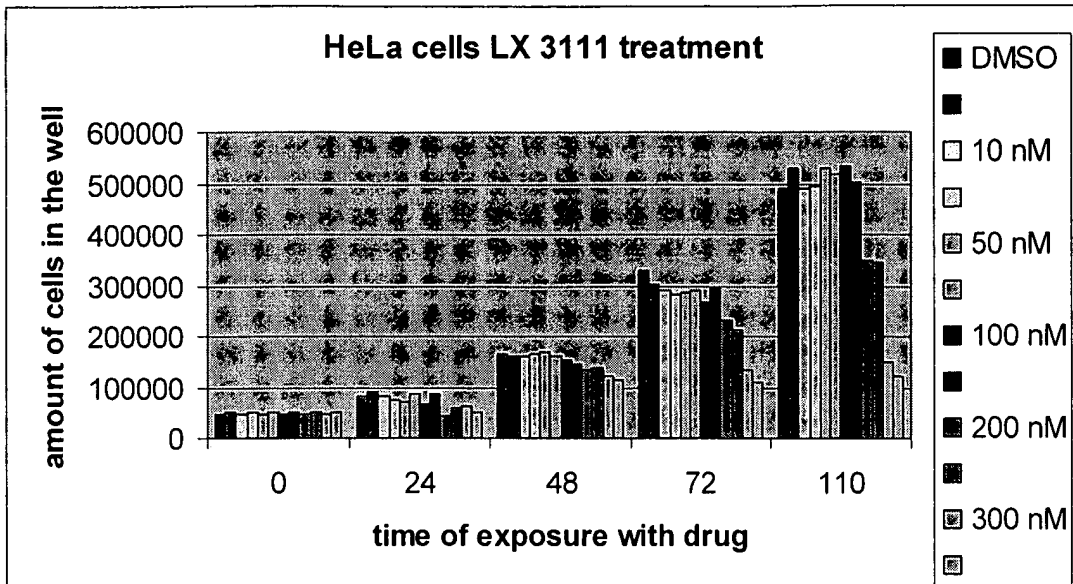


FIG. 75

A



B

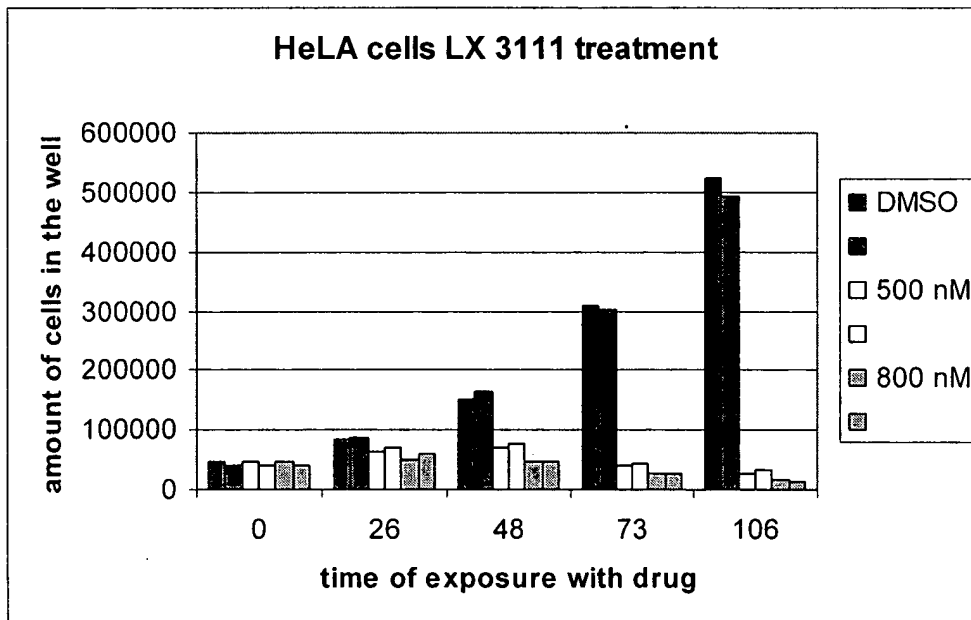


FIG. 76

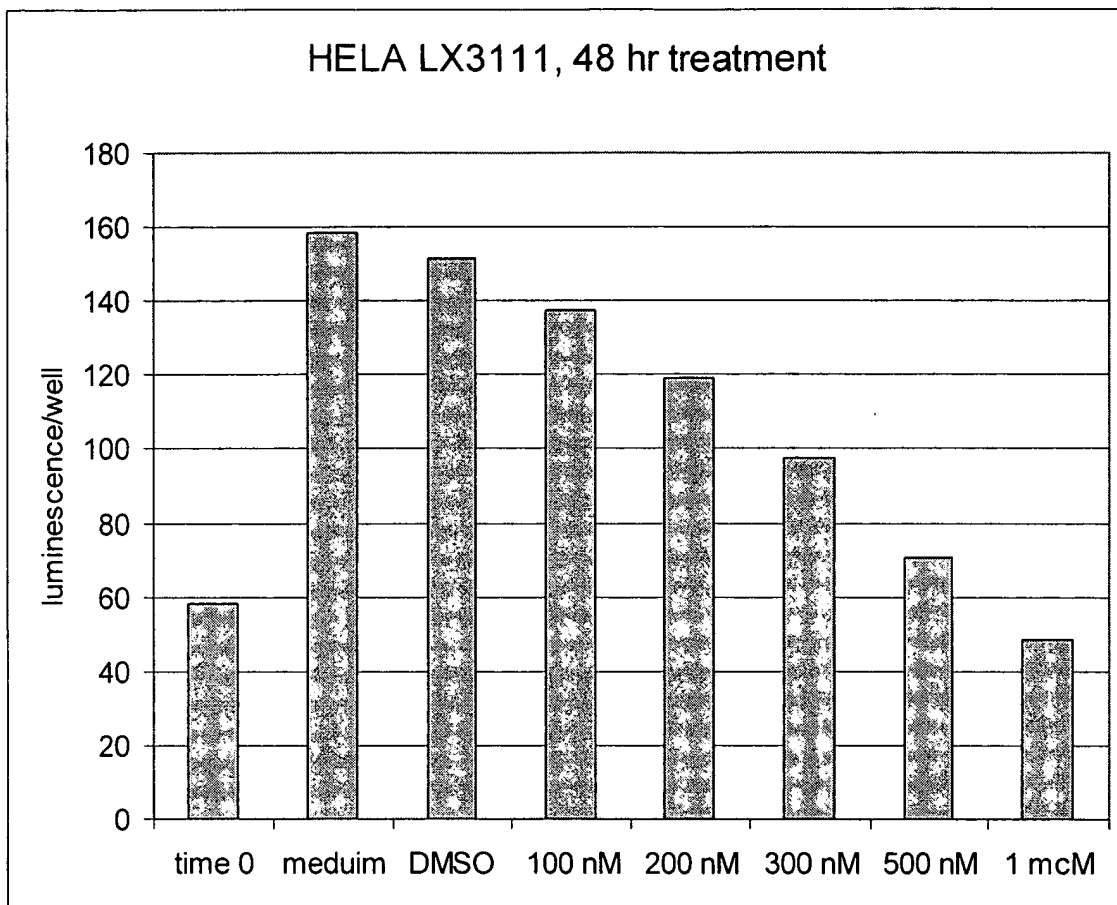
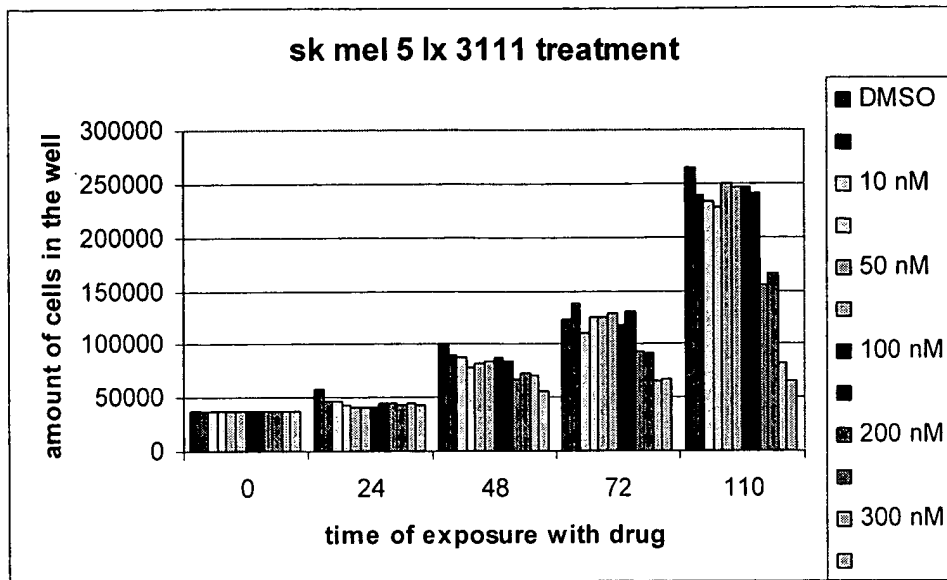


FIG. 77

A



B

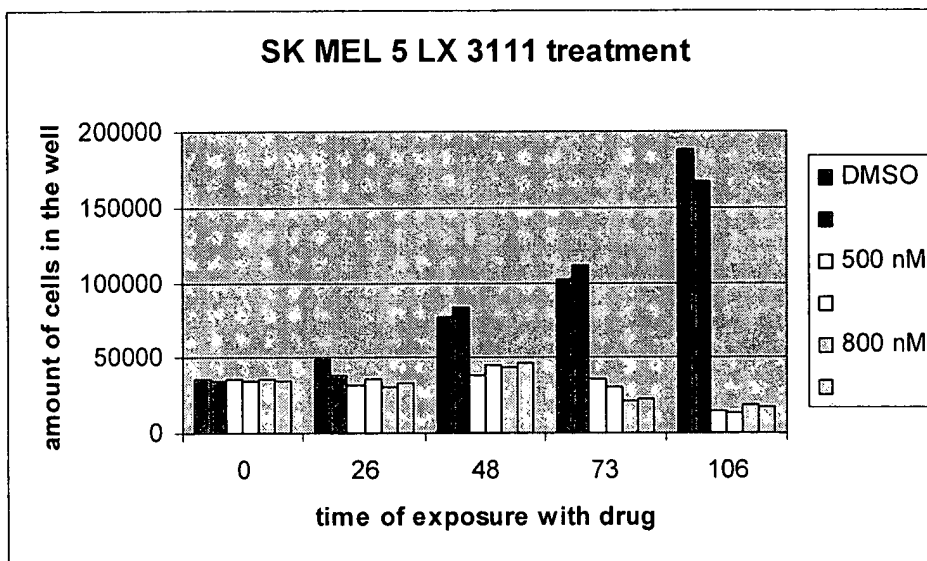


FIG. 78

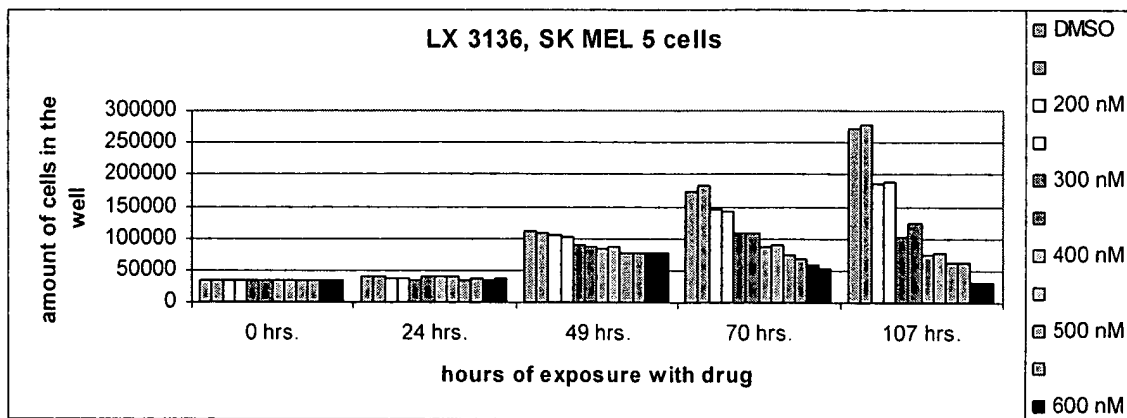


FIG. 79

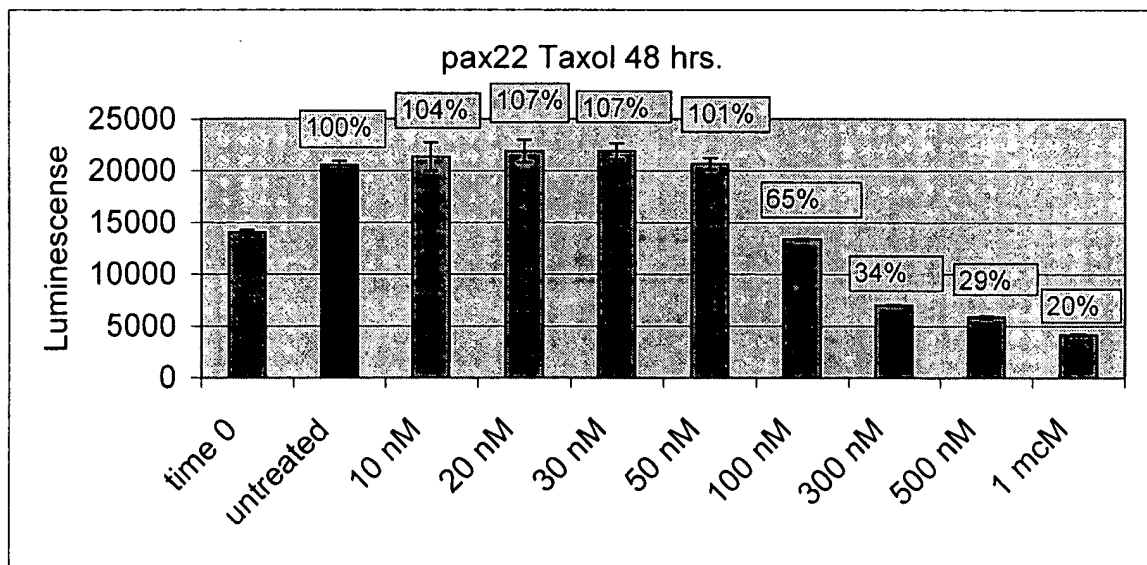
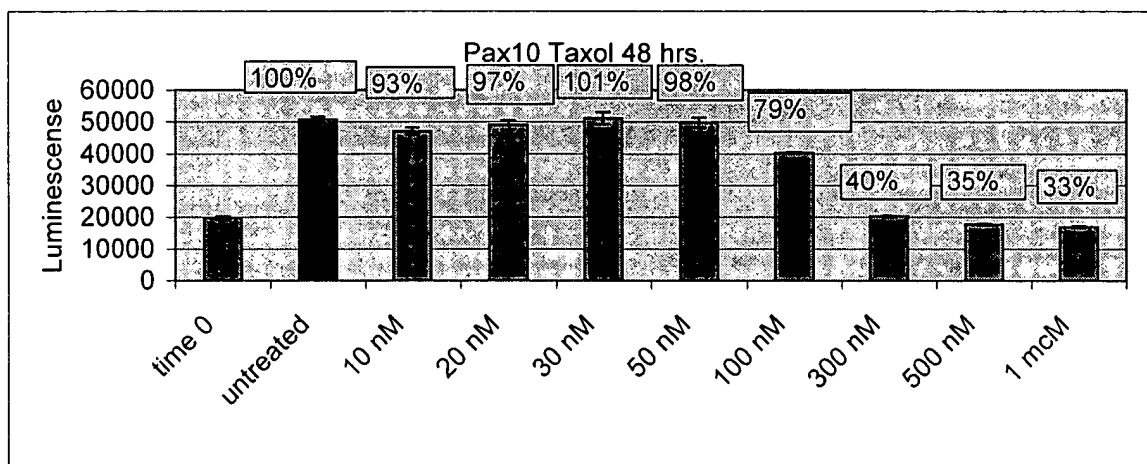
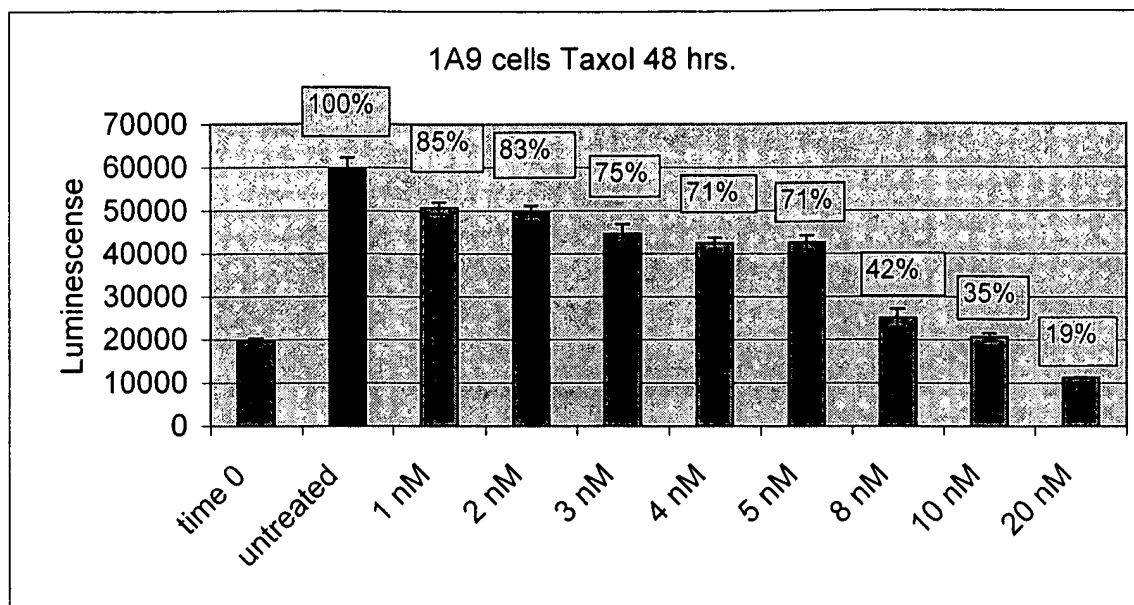


FIG. 80

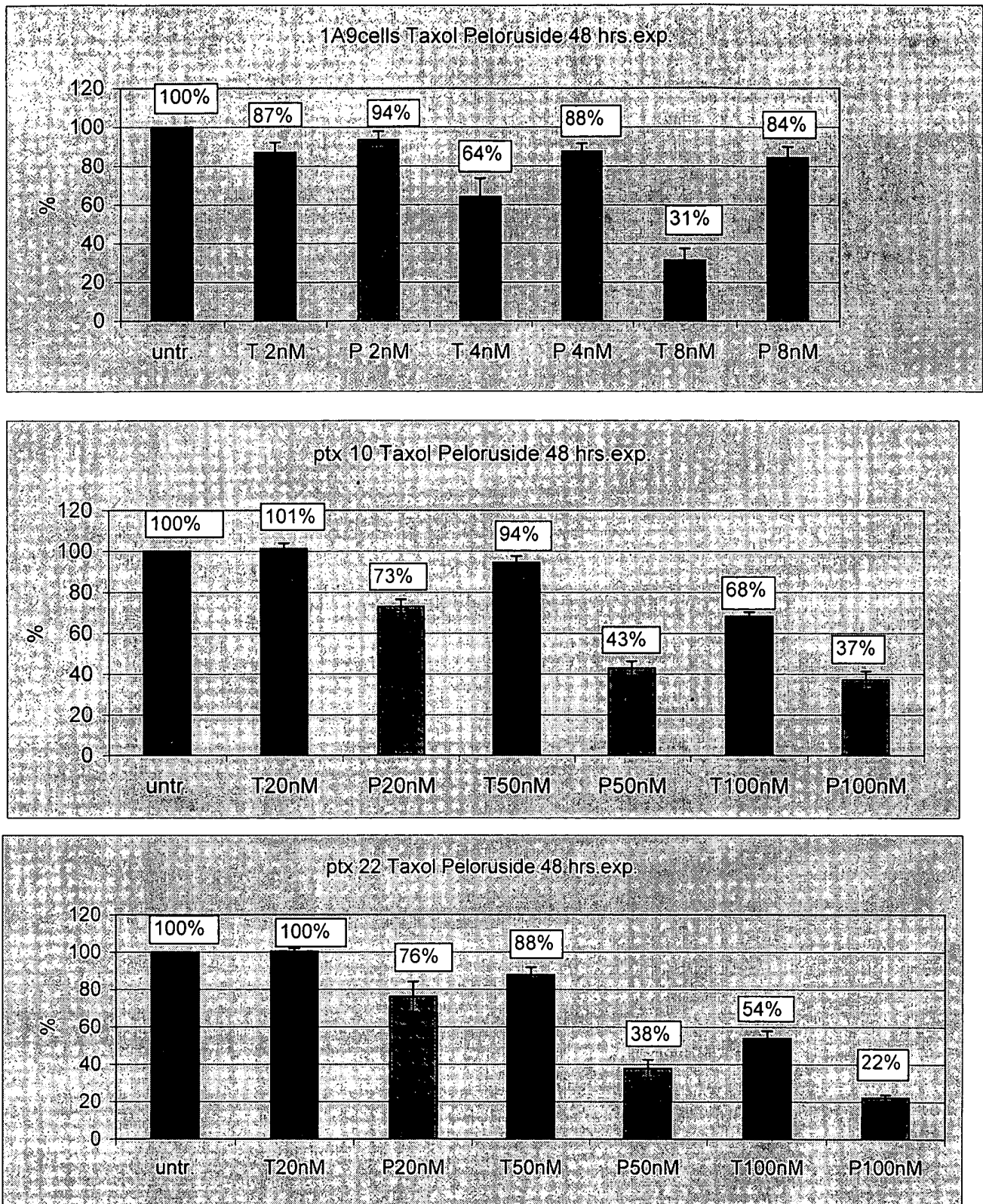


FIG. 81

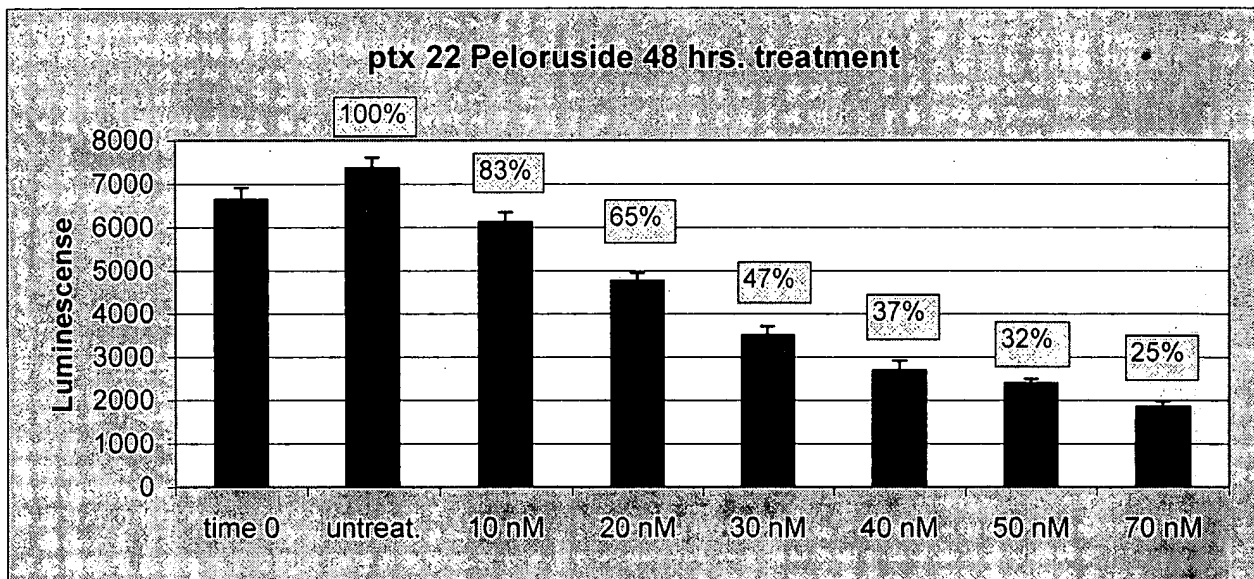
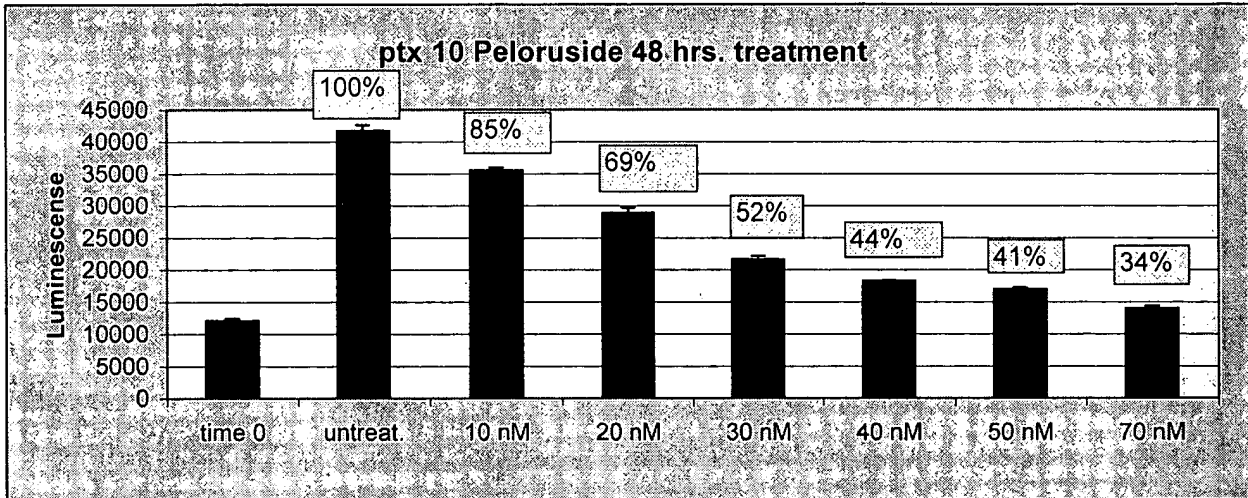
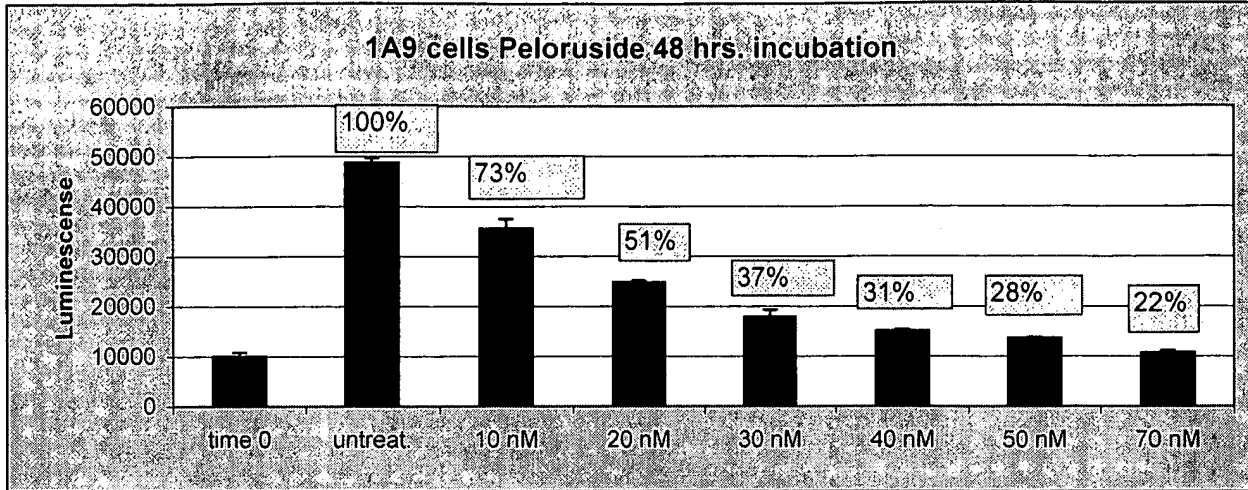


FIG. 82

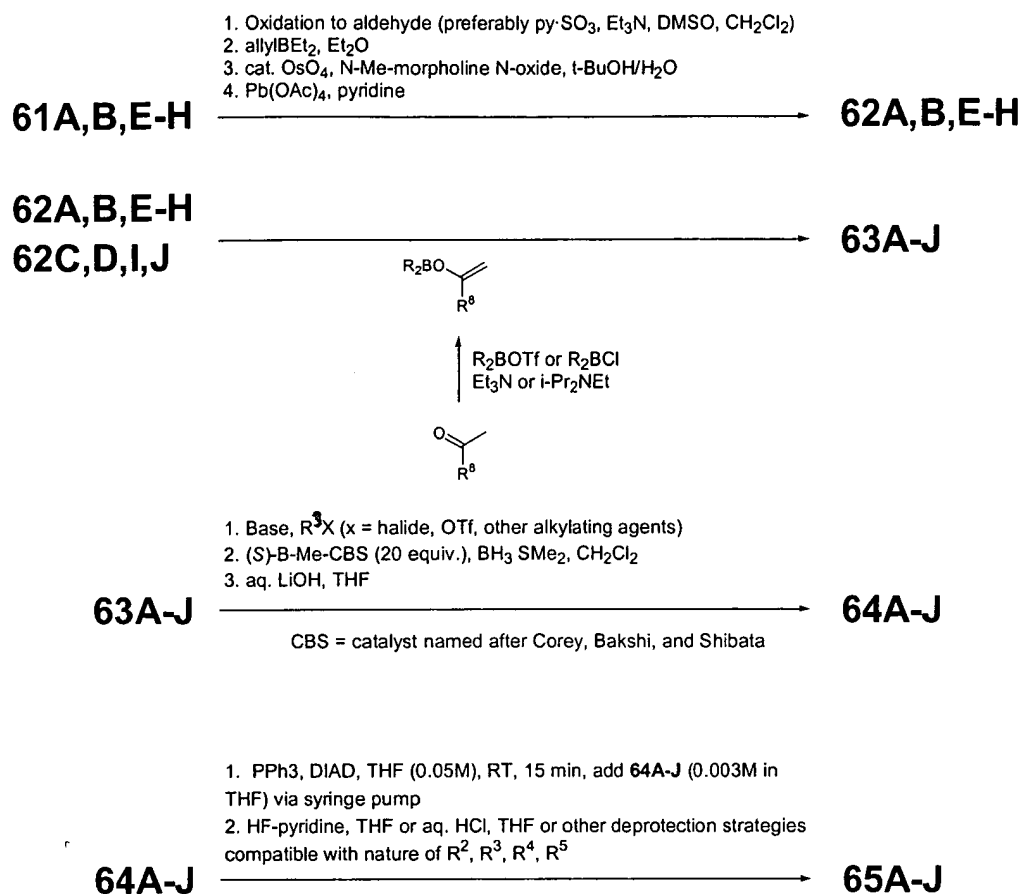
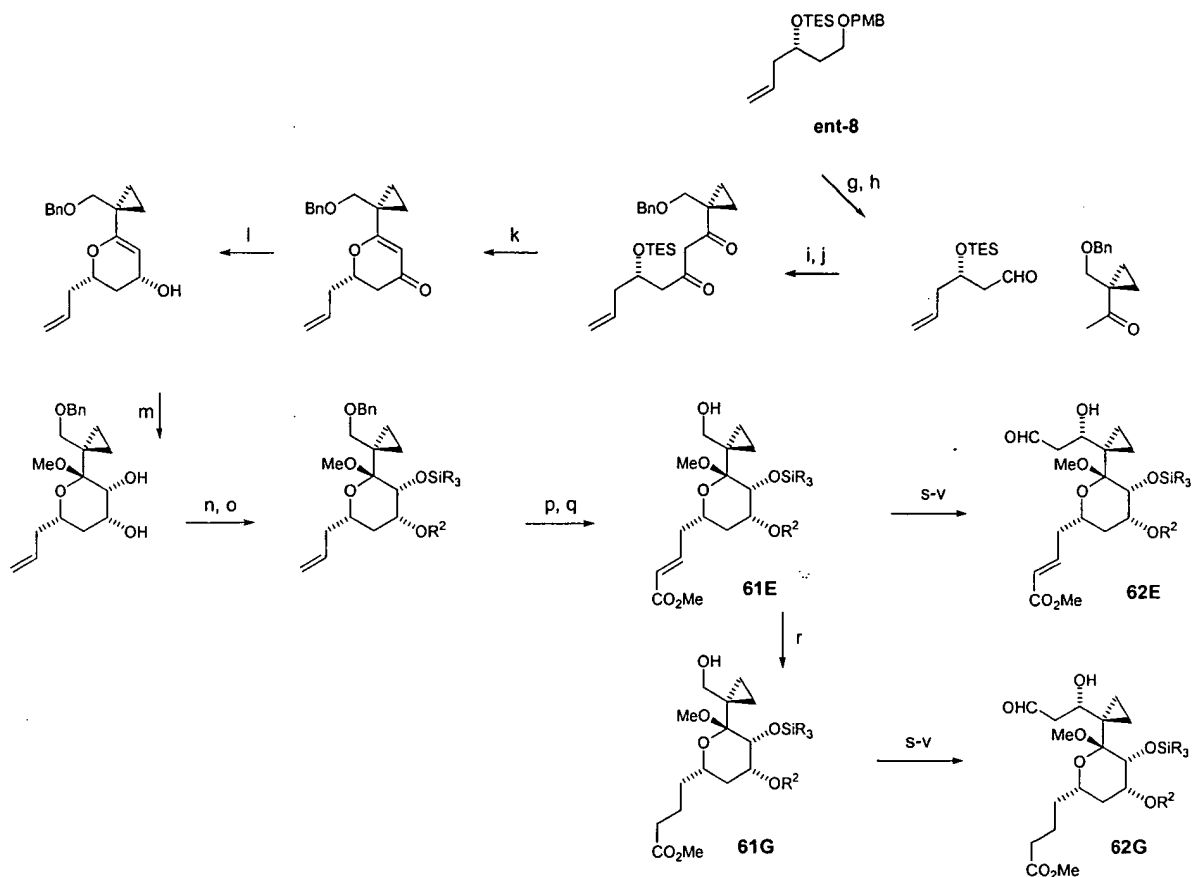
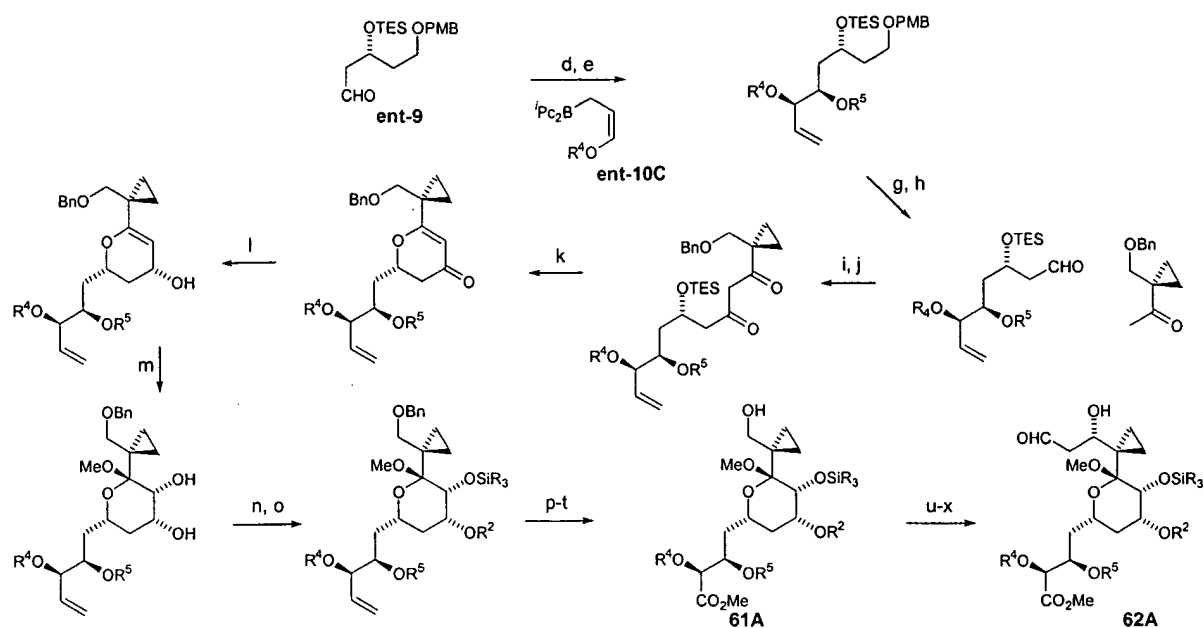


FIG. 83



Reagents and conditions: g) DDQ, CH₂Cl₂/H₂O; h) oxidation to aldehyde; i) LDA, THF, -78°C; j) oxidation to ketone; k) H⁺; l) NaBH₄, CeCl₃·7H₂O, MeOH; m) mCPBA, NaHCO₃, CH₂Cl₂/MeOH; n) base, R₂X; o) R₃SiOTf, 2,6-lutidine; p) LiDBB, THF or Li, naphthalene, THF; q) Ru-alkylidene catalyst (cross metathesis); r) conjugate reduction; s) oxidation to aldehyde; t) allylBEt₂; u) cat. OsO₄, NMO; v) Pb(OAc)₄. PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperoxybenzoic acid, Bn = benzyl.

FIG. 84



Reagents and conditions: d) **ent-10C** (prepared from $R^4OCH_2CH=CH_2$, $sBuLi$, THF, $-78^\circ C$, 15 min, then $(-)-lpc_2BOMe$, $-78^\circ C$), then **ent-9**, $-95^\circ C$, 30% H_2O_2 , NaOH; e) base R_5X ; g) DDQ, CH_2Cl_2/H_2O ; h) oxidation to aldehyde; i) LDA, THF; j) oxidation to ketone; k) H^+ ; l) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH; m) mCPBA, $NaHCO_3$, $CH_2Cl_2/MeOH$; n) base, R_2X ; o) TESOTf, 2,6-lutidine, CH_2Cl_2 ; p) cat. OsO_4 , NMO, acetone/ H_2O ; q) $Pb(OAc)_4$, pyridine; r) $NaClO_2$, NaH_2PO_4 , 2-Me-2-butene, $tBuOH/H_2O$; s) CH_2N_2 ; t) hydrogenolysis; u) oxidation to aldehyde; v) allyl BEt_2 ; w) cat. OsO_4 , NMO; x) $Pb(OAc)_4$. PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, lpc = isopinocampheyl, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

FIG. 85

R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

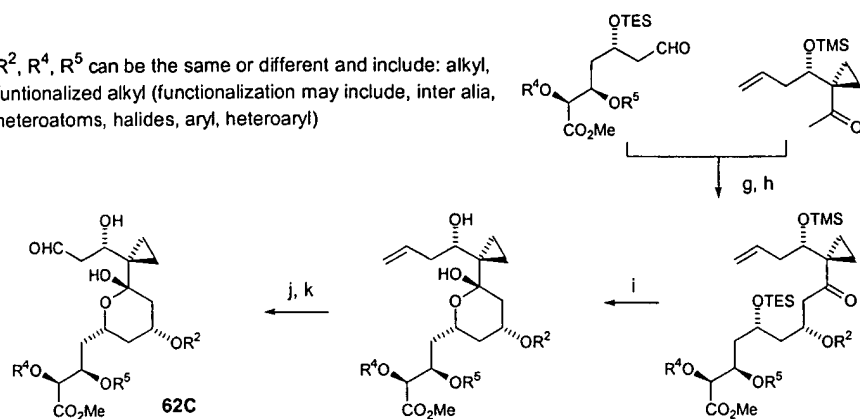
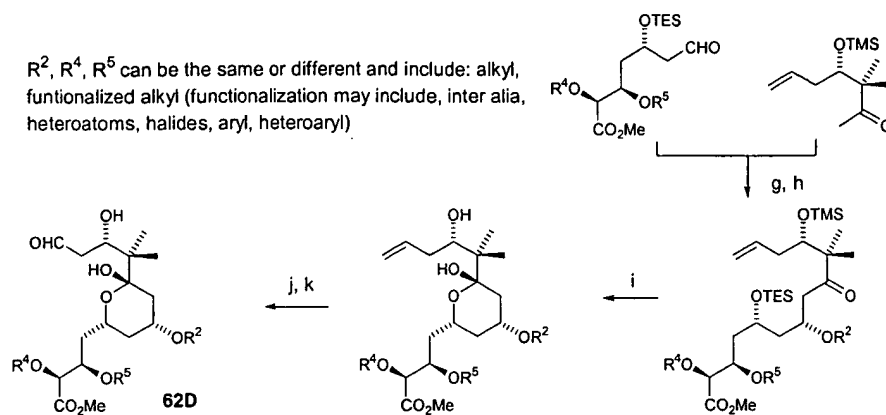


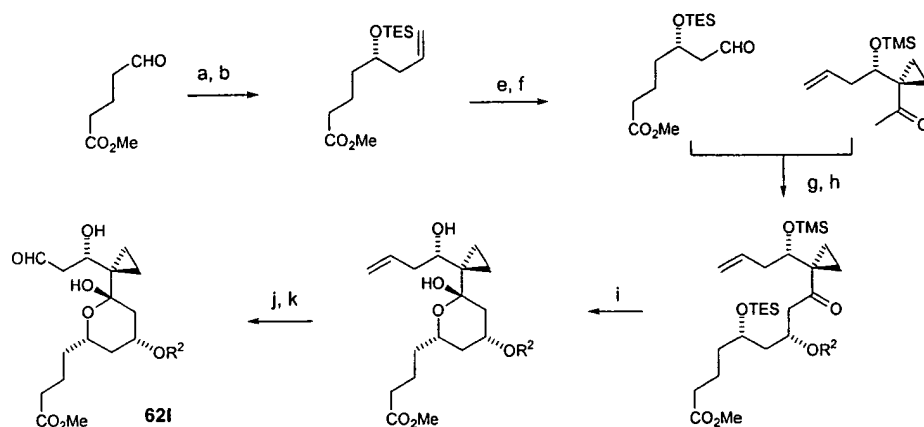
FIG. 86

R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)



Reagents and conditions: g) LDA, THF; h) base R_5X ; i) H^+ ; j) cat. OsO₄, NMO; k) Pb(OAc)₄. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

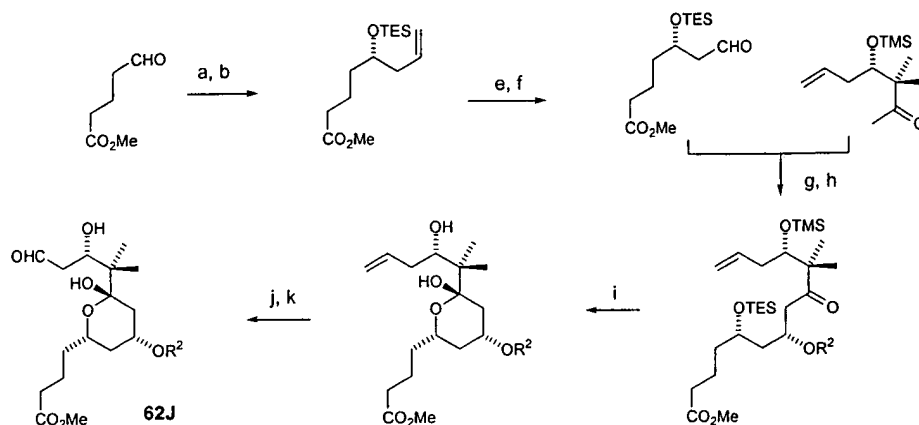
FIG. 87



Reagents and conditions: a) $\text{Ipc}_2\text{Ballyl}$; b) TESCl ; c) cat. OsO_4 , NMO ; d) $\text{Pb}(\text{OAc})_4$; e) base R_5X ; f) H^+ ; g) cat. OsO_4 , NMO ; h) $\text{Pb}(\text{OAc})_4$. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

R^2 can include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

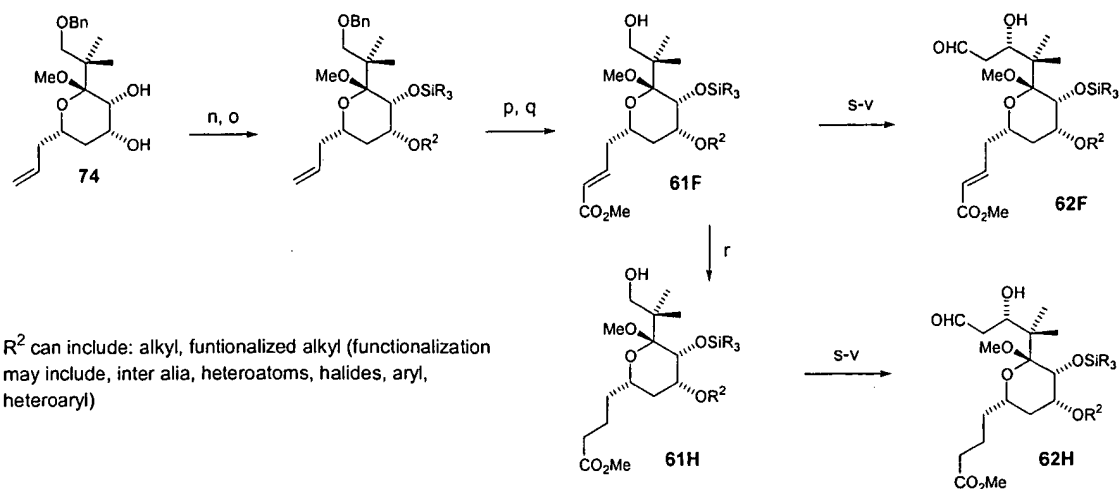
FIG. 88



Reagents and conditions: a) lpc₂Ballyl; b) TESC; c) cat. OsO₄, NMO; d) Pb(OAc)₄; e) base R₅X; f) H⁺; g) cat. OsO₄, NMO; h) Pb(OAc)₄. TMS = trimethylsilyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, LDA = lithium diisopropylamide.

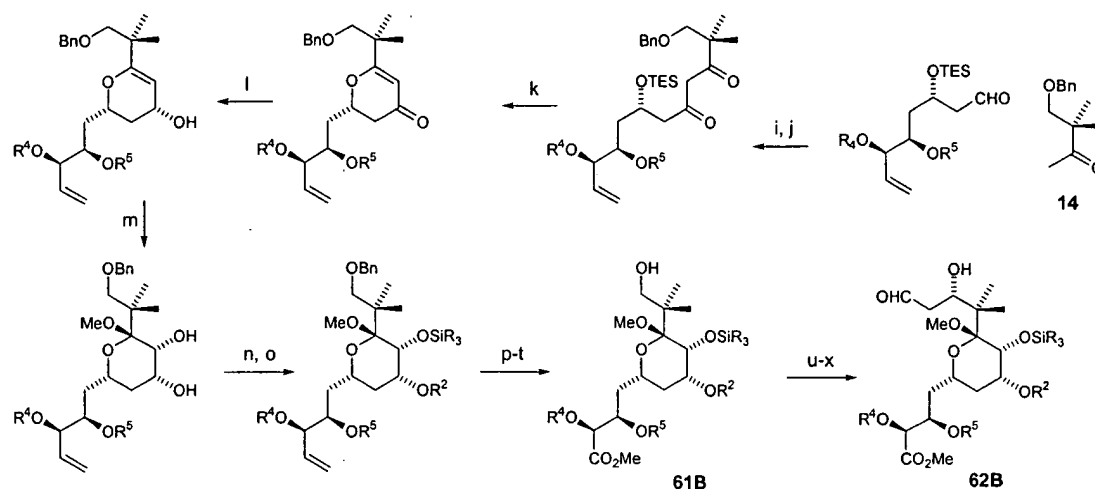
R² can include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

FIG. 89



Reagents and conditions: n) base, R_2X ; o) TESOTf, 2,6-lutidine; p) LiDBB, THf or Li, naphtalene, THF; q) Ru-alkylidene catalyst (cross metathesis); r) conjugate reduction; s) oxidation to aldehyde; t) allylBEt₂; u) cat. OsO₄, NMO; v) Pb(OAc)₄ PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

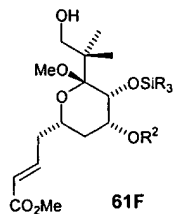
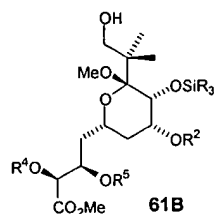
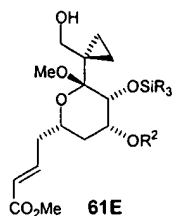
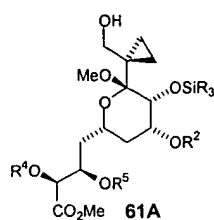
FIG. 90



Reagents and conditions: i) LDA, THF; j) oxidation to ketone; k) H^+ ; l) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH; m) mCPBA, $NaHCO_3$, CH_2Cl_2 /MeOH; n) base, R_2X ; o) TESOTf, 2,6-lutidine, CH_2Cl_2 ; p) cat. OsO_4 , NMO, acetone/ H_2O ; q) $Pb(OAc)_4$, pyridine; r) $NaClO_2$, NaH_2PO_4 , 2-Me-2-butene, $tBuOH/H_2O$; s) CH_2N_2 ; t) hydrogenolysis; u) oxidation to aldehyde; v) allylBEt₂; w) cat. OsO_4 , NMO; x) $Pb(OAc)_4$. PMB = p-methoxybenzyl, TES = triethylsilyl, NMO = 4-methylmorpholine-N-oxide, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, LDA = lithium diisopropylamide, mCPBA = m-chloroperbenzoic acid, Bn = benzyl.

R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

FIG. 91



R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

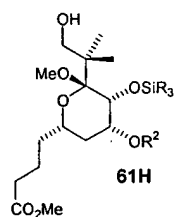
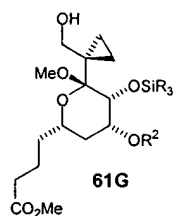
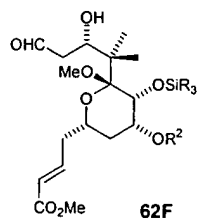
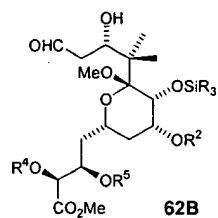
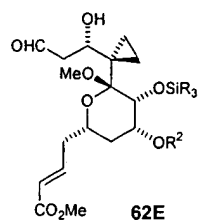
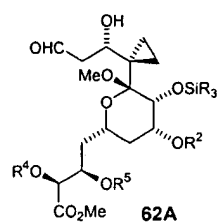


FIG. 92



R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl)

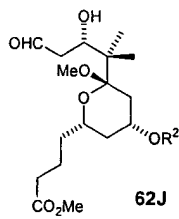
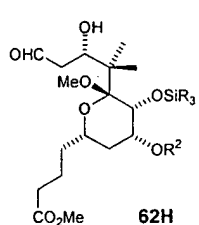
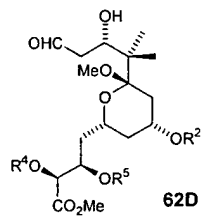
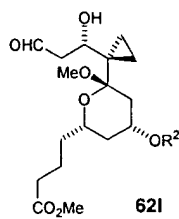
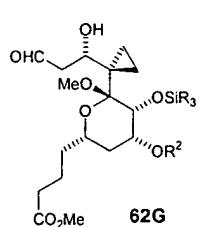
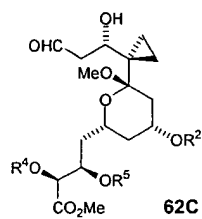
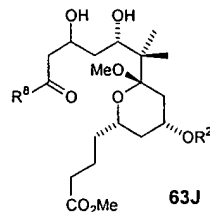
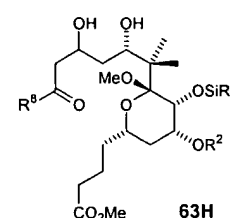
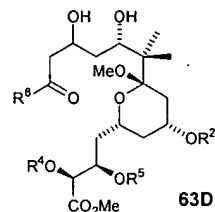
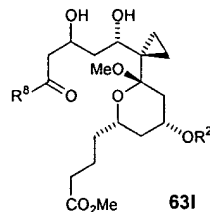
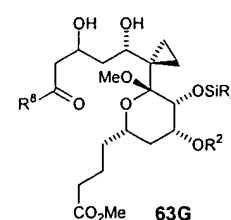
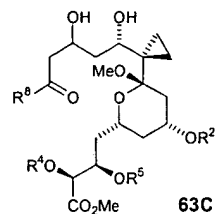
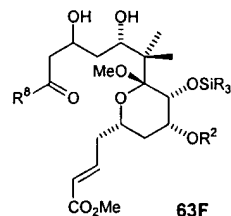
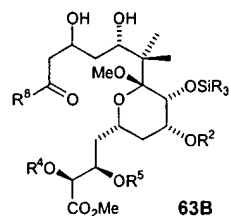
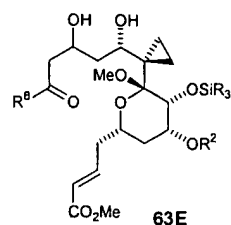
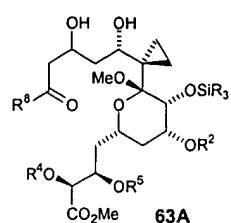
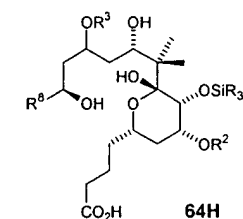
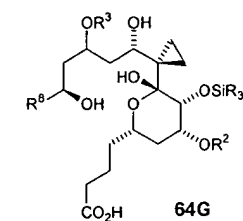
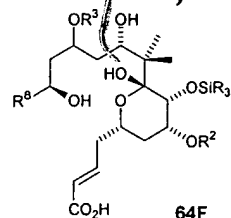
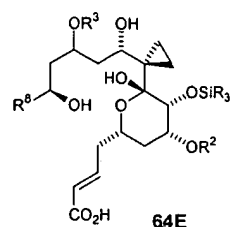
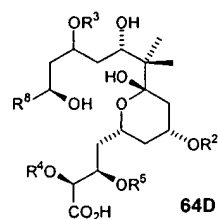
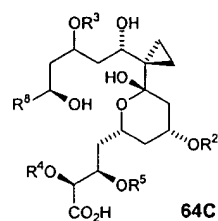
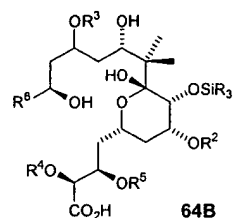
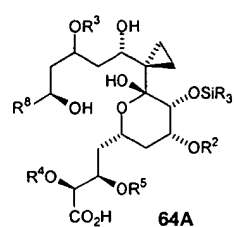


FIG. 93



R^2 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^6 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl).

FIG. 94



R^2 , R^3 , R^4 , R^5 can be the same or different and include: alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^8 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl). The configuration at the carbon bearing the OR^3 substituent can have the *R*- or *S*-configuration.

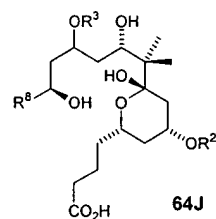
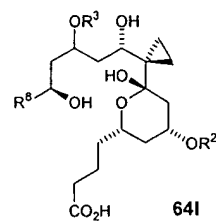
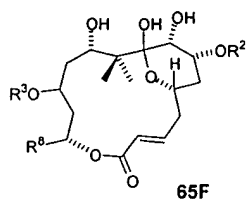
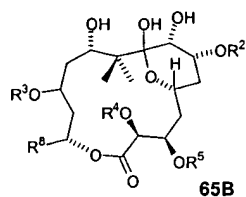
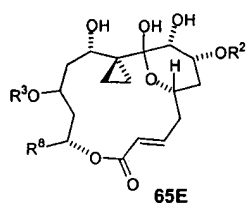
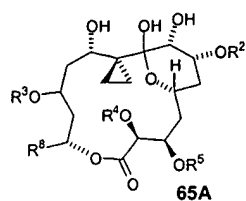


FIG. 95



R^2, R^3, R^4, R^5 can be the same or different and include: H, alkyl, functionalized alkyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl), and where R^8 = aryl, heteroaryl, alkyl, functionalized alkyl, alkenyl, functionalized alkenyl, alkynyl, functionalized alkynyl (functionalization may include, inter alia, heteroatoms, halides, aryl, heteroaryl). The configuration at the carbon bearing the OR^3 substituent can have the *R*- or *S*-configuration

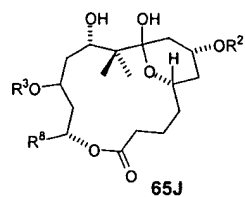
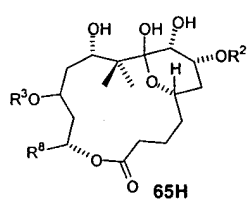
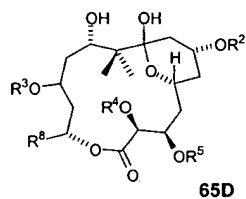
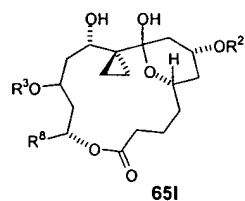
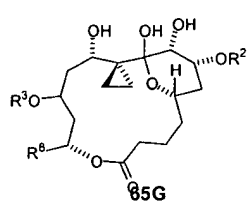
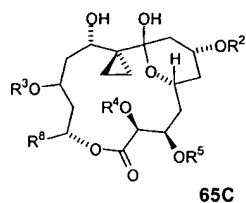


FIG. 96



FIG. 97